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THE ART OF COMPOUNDING

SCOVILLE

THE ART OF COMPOUNDING

A TEXT BOOK FOR STUDENTS

AND

A REFERENCE BOOK FOR PHARMACISTS

AT THE PRESCRIPTION COUNTER

BY

WILBUR L. SCOVILLE, PH.M.

FORMERLY PROFESSOR OF THEORY AND PRACTICE OF PHARMACY IN THE MASSACHUSETTS COLLEGE OF
PHARMACY; MEMBER OF THE EIGHTH AND TENTH COMMITTEES OF REVISION OF THE UNITED
STATES PHARMACOPŒIA AND OF THE SECOND, THIRD AND FOURTH COMMITTEES OF
REVISION OF THE NATIONAL FORMULARY; DIRECTOR OF ANALYTICAL
DEPARTMENT, PARKE, DAVIS & CO.

FIFTH EDITION, REVISED AND ENLARGED
WITH 85 ILLUSTRATIONS

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W. E. RAY
H. W. L. C. S. A.

PRINTED IN U. S. A.
BY THE MAPLE PRESS COMPANY, YORK, PA.

PREFACE

The first edition of this work was published when the author was teaching the subject in the Massachusetts College of Pharmacy. The immediate purpose of the book was to gather together and classify the numerous detailed helps on prescription compounding, then scattered throughout pharmaceutical literature, and to present these, together with a consideration of incompatibilities, in such orderly arrangement as would be most helpful to the student or compounder. Additional data was also secured from experienced dispensers, mostly in eastern Massachusetts, and from other sources.

In presenting the subjects, two purposes were kept in view: first to systematically present the principles underlying each subject, so that the student may understand the reasons as well as the operations of compounding; second to so illustrate and detail the principles by means of prescriptions and official or standard formulas as to show their range and variety of application, and to indicate their practical utility at the prescription counter. The first is given in the text of the chapters, and the second in the prescriptions.

The first edition contained fourteen chapters, with their illustrative prescriptions, and was so well received that a second and revised edition was published two years later. A more complete revision was embodied in a third edition, appearing in 1904, which contained two new chapters: one on Tablets and one on Sterilization and Disinfection.

In the fourth edition, published in 1914, another chapter was added, that on Biological Products. This edition also included a number of illustrations, many of them being of manufacturing operations on the large scale, which the developments of pharmacy has demanded. A number of prescriptions taken from published State Board examinations from various sources, was also included.

This, the fifth edition, has undergone another complete revision, and another chapter is added, that on Adjusted Solutions, in which is considered the needs and methods for adjusting ampul solutions for reaction and isotonicity, of collyria for isotonic conditions, and of colloidal solutions for stability.

The chapter on Biological Products has been entirely rewritten by L. T. Clark, B. S., who is Junior Director of the biological farm and laboratories of Parke Davis & Co. In considering this subject he has

kept in mind the point of view of the pharmacist, and has aimed to present only the pharmaceutical considerations, omitting a discussion of therapeutic values.

This revision has touched every chapter in the book, and material changes and additions have been made in each; the only chapters that show merely minor corrections are those on Nomenclature and Homoeopathic Pharmacy. The chapter on Emulsions has been largely rewritten and now includes the more advanced views on this subject which have been developed by the work of numerous physiological chemists in later years. The chapter on Incompatibilities contains many changes and additions and also shows the bearings of recent chemical developments on pharmaceutical preparations.

A considerable number of prescriptions have been added, all being from the more recent types of prescription practice; also a number of State Board examination prescriptions taken from the later reports.

More than 650 prescriptions are now included as directly illustrative of the principles discussed in the text, and more than 350 additional typify the State Board examinations of a number of different states. A key to these last has been added, as an aid to candidates in preparing for examination.

The original purpose of the book has been adhered to, and the subjects are confined to prescriptions and extemporaneous pharmacy, but the developments of specialized operations has also been recognized, and while the volume remains primarily a text book for students it is also a fairly complete reference book which will be found useful by practicing pharmacists, hospital workers, and perhaps by teachers and physicians.

The author wishes to acknowledge helpful suggestions and formulas by Professor G. A. Bergy. Criticisms or recommendations from any who may use the book are invited. My thanks are also due to Mr. W. M. Chase, formerly associate editor of the *Bulletin of Pharmacy*, for valuable help in proof-reading, and suggestions regarding the printing and composition.

WILBUR L. SCOVILLE.

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THE ART OF COMPOUNDING

CHAPTER I

INTRODUCTORY

"The good of a book is not in the facts that can be got out of it, but in the resonance it awakens in our own minds. A book may strike out of us a thousand things; it may make us know a thousand things it does not itself know."—Carlyle.

One of the chief objects of a technical education is the acquirement of skill.

And skill involves two things: first, mental knowledge and the power to rightly apply it, and second, manual dexterity.

The first comes to us by reading and study, and in the various ways by which the mind receives the thoughts of others in words.

The second involves a knowledge which cannot be put into words, but must come to us through the medium of the five senses. Each of the senses is a channel through which thoughts are conveyed to the mind, and its mission can be fulfilled by no other means. The skillful man is the wholly trained man; one who has not only learned how to apply the knowledge of others and to judge and plan for himself, but who knows also how to execute, and make inanimate things do his bidding.

This double training is essential for the acquirement of skill in all lines of work. In pharmacy, study and reading will give one a correct idea of how to make a pill, or to divide powders, mould suppositories, etc., but manual practice is necessary to enable one to accomplish these operations neatly and expeditiously.

Conversely mechanical dexterity may be acquired so that these operations, when applied to familiar examples, are easy; but unless the principles involved are understood, new combinations are puzzling, and the mechanical dexterity alone is inadequate to their correct preparation.

By study the knowledge and experience of others are made available to us, and we learn to deduce new methods or to newly apply principles. Study has for its object the assimilation of the thoughts of others. To this end the thought involved in the text must first be understood.

Take for instance this sentence: "After a toxic dose the systolic irritation overbalances the diastolic stimulation, and the pulse becomes dicrotic, because the diastole is interrupted by an abortive systole" (U. S. Dispensatory). What idea do these words convey to you? If the meaning of each word is clear, then the sentence as a whole is readily understood; but if any word is not understood,

the significance of the entire sentence is obscured. A dictionary may clear up the meaning, or a course in the physiology of the heart may be necessary for its full understanding.

The student should make it a rule never to leave a sentence until the meaning of every word and of the sentence as a whole is perfectly clear. Then a few repetitions in reading it serve to fix the thought in the memory. But the key to proper study lies in the first careful reading of the lesson, and the comprehension of the significance of every word.

Then for prescription work and the operations of pharmacy there is something beyond this. Study may enable us to see quickly what principles to apply to any mixture, but the physical properties of the compound are still to be known. These, if thoroughly learned, will teach us not only the art of mixing, but also safeguards against mistakes or inferiority in the stock. Drugs should be to the pharmacist like intimate friends, their appearance, habits, likes, and dislikes, all familiar. These are learned by close observation—through the medium of the senses. Let us see how these apply.

Seeing.—This sense is so very important in pharmacy that a special branch is devoted to it—that of Pharmacognosy.

But its application to the compounding of prescriptions is none the less instructive, though so varied that it can hardly be classified into a course. The habit of close observation is not an easy one to acquire, but it is exceedingly useful.

Take the ingredients of any mixture, and look at them separately. Are they clear or cloudy? Is there a deposit upon the side or bottom of the bottle? What are the colors and how do they change? Are they limpid or viscid? Do they appear the same by reflected as by transmitted light? Such questions can only be answered accurately after careful and repeated observations.

Then on mixing observe again.

Do the liquids mix clearly or not? Are streaks or currents formed in the liquid, and what do they denote? Do solids dissolve quickly or slowly? Do they diffuse readily? What changes in color occur? Is there any effervescence or precipitation? etc.

Such observations make an excellent course in physics, and the pharmacist who practices them habitually will never send out a gritty or streaked ointment or suppository, nor an ill-appearing mess of any sort.

It is not necessary that one should be able to describe all that he sees, for these are the thoughts conveyed without words, and, moreover, "it is quite sufficient" (says Professor Markoe), "to recognize your friends when you see them, though you may not be able to make a list or give a description of all of them."

Hearing.—This sense is the least applicable (directly) of any, to pharmacy.

The popping of a cork should suggest a cause to the pharmacist, and it may indicate the need of attention to the bottle.

An acute ear behind the prescription counter may prevent pilfering by kleptomaniac customers, while the sound of running water may bring suspicion to the customer's mind of a cheap ingredient of his prescription.

A crash may denote trouble and loss.

But in general, silence is more indicative of a good dispensing counter than noise, and there are times when a closed ear is better than an open one.

Smelling.—This is a sense which can receive little aid from outside. An odor is absolutely indescribable, except by analogy, and is comprehended only by the nose. The only way to analyze a perfume is by means of an educated nose, and that needs a deal of educating. Most fluids, and many solids, have a characteristic odor by which they can be identified. It should be remembered, however, that a diluted odor is more characteristic than a concentrated one. The most delicate and pleasing perfumes have a more or less harsh and disagreeable odor when concentrated, but on diluting them the pleasing and distinguishing odor is manifested.

Unless a liquid has, normally, only a weak odor, smelling from the bottle is not a good plan. A drop or two allowed to fall upon a piece of filter paper, which is then waved in the air for a moment, will enable us to get the true odor, and also its relative strength.

Another peculiarity of odors is their anæsthetic action upon the olfactory nerve, particularly true of flowers and delicate odors. After a very few minutes the nerve is benumbed, and the odor is no longer perceptible, or ceases to be pleasant. Nor can other odors be distinguished clearly, since "all smell alike," as the over-zealous samplers at the perfume counter sometimes say. For this reason but two or three odors can be learned at a time.

Besides the more characteristic properties developed by dilution of odors, the smelling of strong and pungent bodies like ammonia water, chlorine solutions, essential oil of mustard, strong nitric or hydrochloric acids, etc., from the bottles, is liable to result in unpleasant or even serious results.

Tasting is closely related to smelling, the odor often suggesting the taste.

Like the odors also, taste is oftentimes more characteristic in the diluted than in the concentrated form. A grain of quinine sulphate, for instance, placed upon the tongue, quickly betrays its bitterness, but the same amount dissolved in two and a half pints of water shows also, on being tasted, how intensely bitter the quinine is, without being so persistent and unpleasant.

A grain of strychnine, dissolved in twenty gallons of water, can be tasted distinctly in the solution, and in this diluted condition the distinction between the quinine and the strychnine bitter is more pronounced. Saccharin has a nauseous, metallic taste when placed upon the tongue, but in dilute solution it is intensely sweet and is agreeable. The characteristic taste of the most powerful poisons can be safely ascertained in *highly diluted solutions*, but the solid forms or strong solutions are dangerous, particularly hydrocyanic acid and the cyanides. The degree of dilution must, of course, vary with the diffusibility of the taste and the dose of the substance.

Sometimes the presence of one substance develops or obscures the taste of another.

Thus, a very small proportion of salt or of vinegar makes sugar taste sweeter, while licorice or coffee partially covers the taste of bitter substances.

Efforts are constantly being made to find means of covering the taste of unpleasant substances, and our list of elixirs is one result of such.

The sense of taste also furnishes a means of identifying many substances. We quickly learn that a sour taste indicates an acid or an acidulous salt; a sweet taste may mean sugar or saccharin or glycerin; a bitter taste comes mostly from tonic or cathartic drugs; and an astringent taste may be due to tannic acid or to a salt of aluminum, lead, zinc or copper. Some pharmacists make a habit of tasting mixtures compounded for internal use, to verify their correctness or detect mistakes. This is not so unpleasant a habit, properly applied, as might seem.

A few drugs, when applied to the mouth and throat, produce sensations more akin to the touch than to the taste. Tincture of aconite, highly diluted (one drop to one or two fluidounces of water), produces a tingling sensation and numbness when a teaspoonful of the liquid is held for a minute under the tip of the tongue. The tingling is not apparent for a few moments, but continues for some time. Cocaine produces a numbness quickly, and chloroform first burns, then benumbs.

A tingling or a numbing sensation is produced by a number of drugs. A few drugs, as soap bark and hellebore (and, in unusual cases, aloe and its preparations), cause sneezing, while very rarely an extremely sensitive individual will suffer severely if ipecac be exposed even for a moment within a distance of several yards.

All such sensations are characteristic of their respective causes, and are valuable as a means of testing or as hints of the general properties of the drugs. The quality of a drug or preparation is oftentimes quickly and accurately ascertained from its taste.

Feeling.—Knack—that indescribable something which lightens labor and passes for skill—is mostly an educated sense of touch. There is a peculiar “feel” to a workable pill or suppository mass, an emulsion, powder-mixture, troche, tablet, etc., indeed to all mechanical operations, which tells us what words or pictures or sounds cannot. It must come to us through the nerves, in our operative practice, and once learned it is rarely forgotten. It is this which enables us to weigh, to mix, to mass, to divide, to roll into shape, quickly and well.

The knack of holding large bottles in pouring, of handling graduates, mortars, spatulas, and all the various implements, gracefully and rightly, is acquired through the sense of touch.

We also find that the feeling of many powdered or crystalline substances is characteristic, and a rough test can be made of the quality or purity of many articles in this way. Such tests have served for the detection of gross sophistications, and are of considerable value in comparing samples of chalk, zinc oxide, etc. Some pharmacists always test ointments containing insoluble powders for grittiness, by feeling them before removing from the slab or mortar. Mixed powders are also tested in the same manner, when one ingredient is harder than the others.

These are the purposes of the prescriptions which follow each chapter in the succeeding pages. They are intended for practice as

well as for study. Nor is the manner of mixing the only, or even, from the educational standpoint, the chief thing to be learned. The physical properties of the ingredients and mixtures should be studied, and deductions made from them. It may be discovered that many of them can be mixed in various ways, and further that "there is no dispensing rule but must be applied subject to the control of the judgment and experience of the operator."

CHAPTER II

THE PRESCRIPTION

The prescription is the written order of a physician for a remedy, usually accompanied with directions for its administration to the patient. Its design is to procure for the patient a special remedy, suited to his present condition, and in such quantity as the physician deems needful.

The word prescription is derived from the Latin word *præscribo*, I write before (*præ*, before, and *scribo*, I write or ordain).

THE LANGUAGE of the prescription is almost universally Latin, because (1) Latin is the language of medical science throughout the world. Thus a prescription written in any part of the civilized world, or by a physician of any nationality, may be readily comprehended and correctly compounded by any pharmacist.

(2) The Latin names of medicines are definite and not subject to the changes common in modern languages. Thus, the Latin term *Gaultheria* means a definite plant, understood by botanists and pharmacists everywhere, but the English equivalent, "Wintergreen," might be interpreted *Gaultheria* or *Chimaphila*. Likewise *Serpentaria* means only a particular and known root, but the English term "Snake-root" may be applied to *Serpentaria*, *Cimicifuga*, *Senega*, *Asarum*, or *Eryngium*. Moreover, the vernacular name of a plant is one thing in English, another in French, and still another in German, Italian, Spanish, etc. The use of Latin obviates the necessity of knowing these different names and likewise procures accuracy.

(3) Oftentimes it is desirable that the nature and ingredients of a mixture remain unknown to the patient, and Latin affords secrecy. This last reason should be remembered and respected by the pharmacist, and inquiries regarding the composition and nature of a prescription should be answered with caution. It may be unobjectionable to answer frankly such questions when asked by people of high intelligence and with honorable motives but in most cases an evasive reply, which conveys little or no information, is advisable. Prescriptions often betray secrets which should be zealously guarded, and, in France, it is a criminal offense to expose their contents or nature to outside inquirers.

The prescription is usually written in three parts: (1) the inscription or ingredients; (2) the directions to the compounder; and (3) the signature, or directions for the patient.

The physician's name, or initials, also forms an integral part of the prescription. This is often printed upon the blanks used.

The inscription and directions to the compounder are written in Latin, the signature either in Latin or English; usually in English, since there is no advantage in writing it in Latin, and there may be a disadvantage through an improper interpretation.

The prescription opens with the symbol *R*.

This was probably, in the original, the sign of Jupiter, *J*, placed at the head as a prayer for favor and healing to that deity—such a custom being common in the days of mythology and superstition. It is now generally understood as standing for the imperative form of the Latin verb *recipio*, “I take,” *recipe*, “take thou.”

The ingredients of the prescription then follow, and are grammatically dependent upon this verb *recipe*.

The quantity of each ingredient is a direct object of the verb, and is designated by the accusative case, while the ingredients modify the quantities, and are in the genitive. These are followed by the sign *M* or *M*, standing for the verb *misce*, “mix,” and any directions to the compounder that may be necessary, as—

“*In chartulas xii numero divide*,” divide into twelve small papers (powders); “*fiant in pilulas xx numero*,” let them be made into 20 pills; “*fac suppositoria vi numero*,” make (thou) 6 suppositories; “*fiat unguentum*,” let an ointment be made, etc.

Take a single prescription for illustration:

R. Morphinae Sulphatis.....grana dua.
Sacchari.....drachmam unam.
Misce et divide in chartulas duodecim.
Signatura:—Capiat unam nocte.

Here the verb *recipe* (take) has for its direct object *grana* (grains), which is therefore in the accusative case, and *dua* (two) being a numerical adjective agrees with it. *Sulphatis* being in the genitive case (corresponding to the possessive in English) tells us what the substance of the powder is, and *morphinae*, also in the genitive, modifies *sulphatis*, and the sentence reads literally, “take of the sulphate of morphine, two grains.”

In the next line the verb is again understood, but is not written; it has for its direct object *drachmam* (a drachm, singular) and *unam* (one) agrees with this. Then *sacchari* is in the genitive, and the line reads, “take of sugar one drachm.” This forms the inscription or the first part of the prescription.

Then follows the imperative verb *misce*, mix, joined to the succeeding sentence by the conjunction *et* (and). *Divide* (imperative form of verb, meaning “divide”) tells us that the mixture is to be mixed and divided, and the succeeding words how. *In* is a Latin preposition meaning “into” when followed, as in this case, by the accusative (or “in” when followed by the ablative), and *duodecim* is indeclinable, but agrees with *chartulas*. Then this sentence reads “mix and divide into twelve powders.”

The last part of the prescription, the signature, is in this case also in Latin.

Signatura means “write” or “directions,” the directions being,—*capiat*, subjunctive form of the verb *capio*, and means “let the patient take.” *Unam* (one) is the direct object of *capiat*, and is, therefore, in the accusative, while *nocte* (at night) is in the ablative because it expresses time. This sentence then reads, “let the patient take one (powder) at night.”

In the every-day writing of prescriptions many of the terms and phrases are abbreviated.

Thus *R* stands for *recipe*, *m* for *misce*, *S.* or *Sig.* for *signatura*, and the quantities are designated by signs and Roman numerals.

Abbreviations are not objectionable if not ambiguous, but some are of the latter nature.

A prescription was received in a western state some time ago as follows:

<i>R.</i>	Hyd. chlor.....	℥i
	Mur. hyd.....	gr. ii
	Aquæ.....	℥i.—m.

This should take the prize for ambiguity, for the abbreviations "chlor." and "mur." are synonymous, the second being an old form still in common use, standing for muriate (chloride), muriatic, etc., while "hyd." occurs in both cases. The first line then might stand for "hydrargyri chloridi"—chloride of mercury, and this might be either calomel or corrosive sublimate, or it might stand for hydrate of chloral. The second line, at first thought, would be supposed to mean the same. But the physician really desired in this prescription,

Chloral (hydrate).....	one drachm.
Muriate (hydrochlorate) of hydrastine..	two grains.
Water (distilled).....	one fluidounce.

Further, the abbreviation "hyd." might stand, in different connections, for hydrargyrum, hydrate, hydrochlorate, hydrocyanide, or hydriodate, while "chlor." might be intended for chloride, chlorinated, chlorate, chlorine, chloral, or chloroform.

"Sulph." might stand for sulphur, sulphide, sulphite, or sulphate, and "phos." for phosphorus, phosphide, phosphite, or phosphate.

The Pharmacopoeia and the National Formulary both give official abbreviations which are intended to avoid just such ambiguities.

It may be noted that a knowledge of classical Latin is not a necessity to the pharmacist, but it is a great aid and a stimulus to a wider education and a better understanding of technicalities. Without it the compounder must depend upon the unaided memory, or upon tables of technical terms.

Classical Latin contains but few of the technical terms, but it makes the student familiar with construction, idioms, etc., so that these are more readily learned, remembered, and understood.

RECEIVING THE PRESCRIPTION

It is customary in some of the larger stores to give checks upon receiving a prescription. The checks are numbered or lettered, and the corresponding mark or a duplicate check is written upon or attached to the prescription. This prevents mistakes in delivering the medicines, the check or mark being transferred to the packages as these are prepared.

The prescription should be read carefully and thoroughly. *Make it a rule never to dispense a prescription any part of which is not well understood.*

The character or strength of a mixture often depends upon a single word or sign, and a careful scrutiny is always necessary.

Many pharmacists write the label before beginning to compound the prescription—an excellent practice. This gives time for a second reading or for any hints which may be noted in the directions, and also for thought as to the manner of compounding; moreover, the label then becomes thoroughly dry before being pasted upon the bottle.

The legibility of a prescription is as often as much a matter of experience in the compounder, as of the chirography of the writer.

Dispensers gradually become accustomed to certain combinations, and the presence of one ingredient suggests another, or at least makes the interpretation of a more obscure line easier. They also become familiar with peculiarities in the handwriting of physicians in their locality, and prescriptions which may seem to be mere hieroglyphics to the novice or to dispensers in another town may be simple and plain to them.

So then the ability to decipher a badly-written prescription depends quite as much upon experience in dispensing as upon skill in interpreting badly-formed letters.

If any ambiguity occurs in the prescription, any dangerous doses, undesirable incompatibilities, or any other feature, makes it desirable that the physician should be consulted before the prescription is compounded, the customer should never be made to suspect that anything is wrong. The latter may be dismissed with information that the prescription will require an hour or two to compound, or some such excuse, and the prescription sent to the physician without his (the customer's) knowledge. Faith in both the physician and the pharmacist is an important factor in medical treatment, and it should be fostered at all times.

The doses of powerful remedies should be carefully scrutinized in each case.

Many a life has been saved by the watchfulness of pharmacists in this regard, and the reputation of the physician preserved as well.

On the other hand, the pharmacist is held criminally liable with the physician, by the law, if he compounds and dispenses a prescription containing a fatal amount of poison in a dose.

Unusual doses of powerful drugs are sometimes purposely ordered by physicians for special cases. This is particularly liable to occur with morphine and opium and their preparations. In such cases the physician alone is responsible, provided the dose was ordered thoughtfully.

Several plans for designating such special doses have been proposed, such as drawing a heavy line, for emphasis, under the dose and remedy in question, the writing of the dose in both Roman and Arabic characters, or in both English and Metric systems, the emphasizing of the dose by an exclamation mark (!) or by the letters Q. R. (quantum rectum), etc., and it is to be regretted that some method has not been universally adopted. Occasions frequently arise when from abnormal conditions, extreme pain, or other causes, doses may be needed which in ordinary usage would be dangerous, and delay in compounding these (which are usually wanted quickly for relief) would be avoided many times by some recognized method.

In judging of the safety of a given dose, three things must be taken into account, (1) the age or weight of the patient, (2) the form in which it is given, and (3) the frequency or extent of its repetition.

Doses are usually given in tables, books on posology, etc., as maximum and (sometimes) minimum doses for adults, but even with adults personalities make much difference. As a rule a man will stand a larger dose than a woman, and a heavy muscular man more than a light and nervous one. For children the dose is regulated according to age. Dr. Young's rule, which is frequently used, is, "Divide the age of the child, in years, by the age plus twelve." For example, if the child be three years old, the dose would be $\frac{3}{3+12} = \frac{3}{15}$ or $\frac{1}{5}$, and the dose is therefore one-fifth that of an adult. Another rule is to add 1 to the age in years, and divide by 24,—thus for the same child (3 years old) calculate $\frac{3+1}{24} = \frac{4}{24}$ or $\frac{1}{6}$; the dose then is one-sixth that given to an adult.

It must be remembered that infants and young children are extremely sensitive to morphine and opiates, death resulting at times from seemingly very small doses, and judgment must be used as well as rules.

The form in which the medicine is administered also effects its vigor. Hypodermic injections, bringing the remedy directly and suddenly into the circulation, effect a full action in smaller doses than when the drug is administered in other forms.

Liniments, ointments, suppositories and other external or semi-external remedies, acting by slow and gradual absorption, produce their effects more slowly than when administered by the mouth, and larger doses may, as a rule, be administered in these forms.

Suppositories of strychnine or nux vomica (and ignatia) are an exception here, since strychnine acts very quickly and vigorously when administered through the rectum, and smaller doses are therefore advisable.

Bodies in solution generally act more promptly than when in solid form, and so insoluble forms of medicinal agents may sometimes be used in larger amounts.

Very little difference is noted, however, in the dose of remedies in pill or powder forms and solutions.

The frequency or extent of repetition of a dose is decidedly important with some drugs. Some are fugitive in their action, while others are cumulative.

With opium (morphine) and cocaine, for instance, the action is prompt and soon passes away except with young children, in whom the action is more prolonged as well as more violent. The system quickly becomes accustomed to these, and an increase in dose becomes necessary to produce the desired effect. Such drugs may be given in repeated doses without ill effects other than the establishment of a systemic craving for them, if long continued.

Cumulative drugs, on the other hand, like strychnine, nux vomica and digitalis, do not produce their full effects at once, but gradually accumulate in the system, their action increasing with the drug.

Small, repeated doses may thus give rise, after a time, to symptoms of poisoning similar, though less dangerous, to those produced by a single excessive dose.

A questionable dose of such remedies as these becomes more apprehensive if the mixture contains a large number of doses which are to be taken at frequent intervals.

Veterinary Doses.—Pharmacists are sometimes called upon to advise regarding the doses for animals. In general the doses should correspond to the weight of the animal, but there are some exceptions. Cows are less susceptible to medicines than are horses, though of about the same weight.

The following relative doses will apply in general.

Horses.—8 to 16 times the dose for man.

Cows.—12 to 24 times the dose for man.

Sheep and Goats.— $1\frac{1}{2}$ to $2\frac{1}{2}$ times the dose for man.

Swine.—1 to 2 time the dose for man.

Dogs.—Corresponds to man according to weight.

Cats.— $\frac{1}{4}$ to $\frac{1}{2}$ the dose for man.

There are certain medicines which have peculiar action upon animals, to which attention should be paid.

Opium affects animals quite strongly and should be given in relatively smaller doses than most medicines. Cats are excited by it, and it also causes diarrhoea in them. If given to cats at all, it must be in extremely small doses. Dogs respond to it in a more normal way.

Nux Vomica and Strychnine.—Dogs and cats are very susceptible. A single aloin, belladonna and strychnine pill given to a dog for a cathartic, has resulted in death. Strychnine should be given to these animals very cautiously. Other animals respond normally.

Phenol.—Dogs and cats are extremely susceptible to phenol poisoning. It should not be used on these animals as an antiseptic. Cresol is much safer, but it also should be used cautiously.

Pilocarpine and Jaborandi act as a diaphoretic on horses, but not on other animals.

Vermifuges act on all animals in a way corresponding to the action on man. Young animals are relatively more susceptible. All vermifuges are poisonous and act by virtue of their toxic action on the worms, so must be used cautiously.

The following table of veterinary doses which was published by a "Veterinary Pharmacist" in the British and Colonial Druggist in 1922 may be helpful. Some judgment is needed in interpreting these since a dog weighing 3 or 4 pounds cannot take a dose which would be small for a mastiff weighing 120 pounds. The age, breed, size and general condition must be considered for all veterinary doses.

TABLE OF VETERINARY DOSES

NAME OF DRUG	HORSE	COW	SHEEP OR PIG	DOG	CAT	FOWL
Aconite (tincture)	15-60 ℥	30-120 ℥	15-30 ℥	2-10 ℥	1-6 ℥	1-5 ℥
Æther	1-2 ℥	2-4 ℥	2-6 ℥	10-8 ℥	2-4 ℥	1-4 ℥
Aloe (barb.)	3-8 ℥	1-2 ℥	2-4 ℥	10-100 grs.	5-10 grs.	2-8 grs.
Antim. tart. (alterative)	1-4 ℥	1-4 ℥				
Antim. tart. (emetic)			8-10 grs.	1-4 grs.	1-1 gr.	
Areca, pulv.	1-2 ℥	1-2 ℥	1-1 ℥	15-90 grs.	5-10 grs.	5-10 grs.
Arsenic alb.	5-10 grs.	5-10 grs.	15-2 grs.			
Arsenical solution				2-10 ℥	1-3 ℥	1-2 ℥
Belladonna extract	1-2 ℥	1-2 ℥	5-15 grs.	1-2 grs.	1-1 gr.	
Camphor	1-2 ℥	1-4 ℥	1-1 ℥	5-15 grs.	2-4 grs.	1-2 grs.
Capsici, pulv.	1-2 ℥	1-2 ℥	1-60 grs.	1-5 grs.	1-2 grs.	1-1 gr.
Castor oil	1-1 pt.	1-2 pts.	4-8 ℥	4-4 ℥	1-4 ℥	1-3 ℥
Catechu pulv.	1-4 ℥	1-4 ℥	1-2 ℥	5-30 grs.	3-5 grs.	2-4 grs.
Chlorodyne				2-20 ℥	2-5 ℥	2-5 ℥
Chloroform (anæsthetic)	2-5 ℥	2-5 ℥	1-2 ℥	2-8 ℥	2-4 ℥	1-3 ℥
Chloroform (asthmatic)	1-3 ℥	1-3 ℥	1-1 ℥	2-10 ℥	2-5 ℥	2-4 ℥
Cinchona pulv.	1-1 ℥	1-2 ℥	1-3 ℥	10-60 grs.	10-20 grs.	5-15 grs.
Cod liver oil	2-4 ℥	2-4 ℥	1-2 ℥	1-8 ℥	1-1 ℥	15-30 ℥
Creosotum	10-30 ℥	20-60 ℥	5-15 ℥	1-5 ℥	1-1 ℥	1-1 ℥
Creta præp.	1-2 ℥	1-3 ℥	1-3 ℥	5-30 grs.	2-8 grs.	5-10 grs.
Croton oil	5-15 ℥	10-30 ℥	1-4 ℥	1-3 ℥	1-1 ℥	1-1 ℥
Digitalis, pulv.	10-30 grs.	15-60 grs.	5-10 grs.	1-6 grs.	1-2 grs.	
" tincture	1-3 ℥	1-3 ℥	5-15 ℥	1-10 ℥	1-2 ℥	
Ergot (ext. liq.)	1-1 ℥	1-1 ℥	1-3 ℥	1-2 ℥	5-20 ℥	
Ferri carb. saccharat.				5-20 grs.	2-6 grs.	1-5 grs.
Ferric chlorid Sol.	2-8 ℥	2-8 ℥	10-20 ℥	5-15 ℥	2-6 ℥	2-10 ℥
Ferri sulph.	20-30 grs.	60-90 grs.	5-30 grs.	1-10 grs.	1-2 grs.	1-3 grs.
Filix mas (ext. liq.)				1-20 ℥	1-5 ℥	1-3 ℥
Gentian, pulv.	1-6 ℥	1-2 ℥	20-60 grs.	3-15 grs.	1-5 grs.	1-5 grs.
Ginger, pulv.	2-6 ℥	2-6 ℥	10-30 grs.	5-30 grs.	2-5 grs.	3-6 grs.
Hydrarg. subchlor	15-60 grs.	15-60 grs.	5-20 grs.	1-10 grs.	1-2 grs.	1-3 grs.
H y o s c y a m u s (tinct.)	1-2 ℥	1-2 ℥	1-3 ℥	10-60 ℥	3-6 ℥	
Ipecac, pulv.	1-2 ℥	1-2 ℥	5-20 grs.	1-10 grs.	1-1 gr.	
" vin.				3-15 ℥	2-4 ℥	1-5 ℥
Jalap, pulv.	3-6 ℥	3-6 ℥	2-6 ℥	1-4 ℥	5-20 grs.	10-20 grs.
Juniper, oil	1-2 ℥	1-2 ℥	5-15 ℥	1-10 ℥	1-2 ℥	
Linseed oil	1-2 pts.	1-2 pts.	4-8 ℥	2-3 ℥	30-90 ℥	1-1 ℥
Magnes. sulph.	1-1 lb.	1-1 lbs.	3-6 ℥	1-6 ℥	10-30 grs.	10-60 grs.
Morphia mur.	5-10 grs.	5-10 grs.	1-1 gr.	1-1 gr.	1-1 gr.	1-1 gr.
Nux vomica (tinct.)	1-2 ℥	1-2 ℥	1-3 ℥	2-20 ℥	1-5 ℥	1-3 ℥
Opium, tinct.	1-3 ℥	1-3 ℥	1-4 ℥	3-30 ℥	1-4 ℥	2-6 ℥
Potas. bicarb.	1-2 ℥	1-2 ℥	20-60 grs.	5-30 grs.	2-8 grs.	
Potas. bromid.	2-8 ℥	2-8 ℥	1-2 ℥	2-30 grs.	1-5 grs.	
Potas. chlor.	1-4 ℥	1-4 ℥	10-40 grs.	2-20 grs.	1-5 grs.	2-6 grs.
Potas. iodid.	1-4 ℥	1-4 ℥	15-60 grs.	1-20 grs.	1-3 grs.	1-2 grs.
Potas. nitrat.	1-2 ℥	1-2 ℥	1-4 ℥	2-20 grs.	1-5 grs.	1-4 grs.
Quinine sulph.	1-2 ℥	1-2 ℥	10-20 grs.	1-10 grs.	1-2 grs.	1-3 grs.
Rhubarb, pulv.				5-60 grs.	3-10 grs.	2-5 grs.
Salicylic acid.	2-6 ℥	2-6 ℥	1-2 ℥	3-30 grs.	1-4 grs.	1-3 grs.
Santonin	1-1 ℥	1-1 ℥	5-20 grs.	1-10 grs.	1-2 grs.	1-2 grs.
Sodii bicarb.	1-6 ℥	1-6 ℥	1-2 ℥	5-40 grs.	2-10 grs.	
Sodii salicylat.	1-1 ℥	1-1 ℥	30-60 grs.	2-20 grs.	1-5 grs.	1-2 grs.
Sp. æth. nit.	1-4 ℥	1-4 ℥	1-3 ℥	5-60 ℥	3-10 ℥	
Sp. ammon. co.	1-1 ℥	1-1 ℥	1-3 ℥	5-60 ℥	5-10 ℥	
Strychnine	1-1 grs.	1-1 grs.	1-1 gr.	10-20 gr.	10-20 gr.	10-20 gr.
Sulphur	1-2 ℥	1-2 ℥	3-6 ℥	20-120 grs.	5-10 grs.	5-10 grs.
Sulphur as a laxative	2-4 ℥	2-4 ℥	4-8 ℥	1-8 ℥	30-60 grs.	1-2 ℥
Turpentine	1-2 ℥	1-2 ℥	1-2 ℥	5-60 ℥	2-5 ℥	

The difference between a minim and a drop should also be borne in mind in figuring doses. A minim is always a sixtieth part of a fluidrachm regardless of the character of the substance, while a drop varies from a forty-fifth to a two-hundred-and-fiftieth part, according to the surface tension of the fluid. Aqueous fluids usually measure from 45 to 70 drops to the fluidrachm; alcoholic liquids, 100 to 150 drops; ethereal liquids, 150 to 250 drops; and volatile oils, 110 to 145 drops to the fluidrachm. The size of the drops will vary, in the same liquid, with the shape and character of the vessel from which they are dropped, particularly as regards the edge or lip, with the rate of dropping and, to some extent, with the temperature.

With a view to securing uniformity in the size of drops on the same liquid, the Brussel's Conference of 1902 adopted a normal drop-counter which was recommended for adoption by the various Pharmacopœias.

This **normal drop counter** shall have an exit with an external diameter of 3 millimeters, and shall discharge drops of distilled water at 15° C. of such a size that 20 drops shall weigh 1 gram.

Since drops are formed by the surface tension of the fluid, it is the external surface which determines the size of the drop, not the bore of the tube. But in order to secure absolute uniformity the external diameter must be exactly 3 millimeters, the tube must be held vertical, the lip must be absolutely clean (a very slight trace of grease making a considerable difference), the temperature of the liquid must be right, and the column of liquid flowing down the tube must be uniform in pressure. These considerations, as well as the standard adopted by the Brussel's Conference—drops per gram, instead of drops per cc.—which is in accordance with the Continental custom of weighing liquids for prescriptions instead of measuring them, have thus far discouraged adoption by the United States Pharmacopœia, but when liquids are to be measured in drops a normal drop-counter is to be preferred. There are such droppers on the market, as the Eschbaum Normal Dropper, the Lamprecht Patent Dropping Flask, etc. But a dropper can easily be made from a pipette or dropping-tube, by simply adjusting the tip to an external diameter of exactly 3 millimeters by drawing out or filing off, as the case may require. Ordinarily filing or grinding the tip down to this size is all that is needed.

Drops obtained from such a dropper will have some degree of uniformity.

The following table is calculated (except the first column) from a table showing the size of drops of the articles mentioned, obtained at 15° C. by C. P. Wimmer and L. Roon, (*Journal*, A. Ph. A., Dec. 1913, p. 1537).

TABLE OF THE NUMBER OF DROPS OBTAINED FROM A STANDARD DROPPER

As Recommended by the Brussels Conference, Temperature 15° C.

Liquid	Drops per gram	Drops per C.c.	Drops per fluid drachm	Drops per minim
Distilled Water.....	20.0	22.2	81.5	1.36
Acid, Hydrochloric.....	19.5	23.8	88.0	1.46
Acid, Hydrocyanic, Diluted.....	20.0	22.2	81.5	1.36
Acid, Nitric.....	22.9	40.0	148.0	2.46
Alcohol.....	65.5	50.0	185.0	3.10
Chloroform.....	58.8	100.0	370.0	6.16
Creosote.....	37.4	45.5	161.0	2.70
Ether.....	90.0	66.5	246.0	4.10
Fluidextract Belladonna.....	55.2	50.0	185.0	3.10
Fluidextract Ergot.....	52.6	50.0	185.0	3.10
Glycerin.....	23.1	33.3	123.0	2.05
Guaiacol.....	38.1	43.5	161.0	2.70
Oil Sandalwood.....	41.5	50.0	185.0	3.10
Oil Wintergreen, Synthetic.....	40.6	50.0	185.0	3.10
Phenol, Liquefied.....	35.5	40.0	148.0	2.46
Solution, Donovan's.....	19.7	22.2	81.5	1.36
Solution Arsenous Acid.....	19.3	22.2	81.5	1.36
Solution Iodine Compound.....	32.0	40.0	148.0	2.46
Solution Potass. Arsenite.....	21.1	22.2	81.5	1.36
Solution Potass. Bromide, 10%.....	20.0	20.0	74.0	1.23
Solution Potass. Iodide, 50%.....	18.7	28.6	106.0	1.76
Spirit Ammonia Aromatic.....	57.3	50.0	185.0	3.10
Spirit Nitrous Ether.....	65.5	59.0	218.0	3.63
Syrup Ferrous Iodide.....	18.9	25.0	92.5	1.54
Tincture Aconite.....	56.3	50.0	185.0	3.10
Tincture Digitalis.....	48.1	50.0	185.0	3.10
Tincture Ferric Chloride.....	53.3	55.5	205.0	3.41
Tincture Hyoscyamus.....	50.8	50.0	185.0	3.16
Tincture Iodine.....	63.3	66.5	246.0	4.10
Tincture Nux Vomica.....	57.3	50.0	185.0	3.10
Tincture Opium.....	50.9	50.0	185.0	3.10
Tincture Opium, Camphorated....	50.9	50.0	185.0	3.10
Tincture Strophanthus.....	57.2	50.0	185.0	3.10
Water, Bitter Almond.....	29.3	27.0	100.0	1.66

In considering **the manner of compounding**, the first thought should be the aim of the prescriber. To interpret this intelligently a general idea of the uses of medicine should be had, so that minor changes may be suggested if improvements can be secured thereby. Criticisms or suggestions as to the therapeutic action of remedies should never be indulged in, but hints toward better pharmaceutical preparations are often welcomed.

Incompatibilities should receive full attention, and be avoided whenever possible.

Always aim at a clear mixture, or, where this is impossible, at a mixture in which any insoluble substance can be evenly diffused by gentle shaking.

Besides this, the proper use of tools should receive attention. Graduates, mortars, spatulas, etc., should be used freely, but not needlessly.

"A good dispenser," says Mr. Ince, "leaves few traces of his work behind him."

The avoidance of incompatibilities and the proper measuring or mixing of powerful remedies is always first, but beyond this the following of a resinous or sticky tincture in the graduate by an alcoholic liquid or of a syrup or mucilage by water, or any successive order which tends to leave the utensils in a less sticky or dirty condition, is as much an evidence of skill and thoughtfulness as the appearance of the mixture itself.

Containers should be chosen to fit as closely as possible the finished mixture.

Liniments should be dispensed in poison bottles, but powerful and poisonous preparations, which are usually dispensed in these when sold without prescription, are preferably dispensed in the common white bottles when ordered on prescriptions, the dose being plainly marked on the label. If the word "poison" is to appear also upon the label, a poison bottle may be used, but frequently the physician does not wish that the dangerous properties of the remedy shall be known to the patient.

Powders are best dispensed in boxes or bottles, whether divided or not. Those which change easily in the air, as the granular effervescing powders, should always be dispensed in wide-mouthed bottles.

In fitting stoppers to bottles, choose a cork which is a little too large rather than one which is small. The latter is apt to get crowded so far into the neck that a hold cannot be secured upon it with the fingers, and a cork-screw or some implement is necessary for its withdrawal; or it may even be crowded into the bottle. Either condition is inconvenient and very annoying in a sick room; moreover it is needless. A cork which is a trifle large is easily reduced by means of the cork-press, and is more agreeable to the patient or nurse. Cork-presses are made for use, not for ornament.

Checking.—After the compounding and labeling of the prescription, a system of checking is followed in the best pharmacies.

Another clerk takes the written prescription and reads it aloud, the compounder following the reading and mentally reviewing the process of compounding. Or the compounder may state what he has compounded, from memory, while the checking clerk scrutinizes the prescription. This calls attention to inaccuracies of the compounder in reading, or to omissions, wrong remedies, etc., during the compounding, thus lessening the liability to mistakes.

Many other plans for preventing mistakes in compounding have been proposed, and are practiced to some extent, such as the aggregation in one spot on the prescription counter of the original containers of all materials used, so that they may again be referred to; the use of poison closets, alarms, etc.; the frequent changing of order upon the prescription counter, so that the grasping of any material does not become habitual from long familiarity with its relative position.

All such plans have their advocates, and there are objections to all, but a system of checking by another, as above mentioned, is in general favor.

Mistakes of all kinds are best avoided by ATTENTION.—Rarely is a mistake made in dispensing when the compounder has the possibility of a mistake in mind. The danger comes when the attention

is divided between the prescription at hand and some foreign subject,—the latter receiving the greater portion of thought,—or when the prescription is not completely understood, and an unwarranted venture is assumed. *Mistakes are always a personal factor* and are best avoided by personal care.

The compounder should (1) Refuse to divide his attention when compounding. If attention to another matter is demanded, it is better to note your position on the prescription at hand, then leave it absolutely for the necessary time, than to attempt to attend to both at the same time.

(2) Thoroughly read, and be sure you understand, every prescription before attempting to dispense it.

(3) When compounding, observe the label of every container used, at least *three times*: Once when taking it from the shelf or drawer; a second time, just before weighing or measuring; and a third time, before returning it to its proper place.

(4) Do not relax your attention until the medicine is in the customer's hands and the prescription properly filed away. When two or more prescriptions are compounded for the same person at the same time, the labels are liable to get mixed unless care is taken to prevent. Serious consequences may follow a mistake of this nature.

Methods of filing prescriptions vary with individual opinions. The method of pasting the original prescription in a book kept for that purpose, has the advantage of preserving the original, which may be a matter of some importance, but is not so neat, and any peculiarities or obscurities in a given prescription must be deciphered by each clerk individually, unless re-written or marked in some way. New clerks are thus forced to struggle, at times, with unfamiliar writing, and with less opportunity for assistance than is allowed with new prescriptions.

The method of copying each prescription into a special book is free from these objections, but any mistake in the first reading, or in re-writing, is perpetuated, and the reference to the original may be impossible.

Whatever method is adopted, four things should appear on each prescription beside the data upon the original. The number, the selling-price of the medicine, the date (and name of the patient), and, in cases of difficulty, the order or manner of mixing, and any special manipulations which have been followed.

The purposes of the number and selling-price are obvious. The date and name of the patient make it possible to find any prescription, at any time, in case the number has been lost. This is a convenience which is due to, and will be appreciated by, the customer.

The data regarding methods of mixing and manipulations insure uniformity in the product, and obviate suspicions on the part of the customer.

The ownership of the prescription is a mooted question, which is best settled by the laws of courtesy and personal judgment. In one of the leading pharmacies of Boston the original prescription is never returned (if compounded), though copies are given when requested.

The reason given for this procedure is that the original prescription is taken as legal evidence in cases of mistakes or any legal charge,

while copies of the prescription have no standing in law. Lawsuits have been prevented by possession of the original.

In another prominent store the original prescription is always returned, and only a copy is preserved.

Probably the location of the store and the character of the trade have as much influence as any factor in such questions.

Perhaps very few stores, if any, refuse to give at least a copy of the prescription to the original possessor, when requested, but other persons should be refused, as a rule.

The renewal of prescriptions is also a question for individual judgment except in the case of prescriptions containing narcotics or liquors, which are restricted by law.

In the majority of cases renewals are expected and granted, on demand, but occasions sometimes arise when a single vial-full is all that is needed or advisable. The notion that a medicine "can do no harm, if it does no good," is in most cases erroneous, sometimes very decidedly so. Moreover, the pharmacist should remember that such conditions as are found in opium or cocaine habitues (not to say drunkards), often originate in the use of a prescription containing one of these drugs in some form, originally prescribed for a legitimate purpose, but renewed from time to time until the habit is established.

These conditions can be prevented by the pharmacist, if he exercises watchfulness.

Some method of marking prescriptions by the physician, to prohibit renewal, has often been advocated, and is certainly desirable.

Narcotic and liquor prescriptions require special treatment in order to comply with the laws governing the dispensing of these articles. Rulings of government officials which apply to these are subject to change at any time, and the laws vary in different states, so that no summary of these is in place in this book. But it must be borne in mind that prescriptions calling for potable liquors can only be dispensed when written on special blanks supplied by government officials, and that these as well as all narcotic prescriptions must contain the name, office address and registry number of the prescriber, the date when written, name of patient, and signature of the prescriber in full. Such prescriptions must be filed separately, and must not be renewed. Other regulations call for records concerning the stock and dispensing of liquors and narcotics, for caution in receiving and dispensing, for the conditions under which they can be dispensed and the forms to be kept are supplied and must be honored. These regulations are changed occasionally and the pharmacist must keep posted regarding them.

GENERAL SUGGESTIONS

Invite customers to be seated while waiting for a prescription.

Study the prescription out of sight. Customers always think that the prescription is faultless and will suspect ignorance or incapability on the part of the compounder if he does not appear to understand it immediately.

Consult reference books freely, remembering that he is best educated who knows where and how to find information when he wants it. Education does not consist in the cramming of isolated facts, but in the power to apply principles.

If any part of the prescription is ambiguous, study the remainder to see if it cannot be revealed thereby. Oftentimes the directions will give a reliable clue to an ambiguous ingredient or quantity. Note the dots over the line as well as the marks underneath, in the quantity signs. Two j's may be so made as to appear like a v; the presence or absence of two dots over the line will settle the question in most cases.

A teaspoonful is usually figured as one drachm, but a fluidounce will commonly yield six or seven teaspoonful doses; rarely eight.

Two drachms may be written as two teaspoonfuls or as a dessert-spoonful. Don't write "teaspoonsful."

Four drachms is a tablespoonful.

Two ounces means a wineglassful, four ounces a teacupful and eight ounces a tumblerful.

Be cautious about questioning the patient, lest he suspect both you and the doctor.

Don't be a catpaw for curious information concerning the doctor. Allay suspicion when you can, but do not encourage it. If asked what the ingredients are, give Latin, German or other obscure names. If questioned concerning its uses, say that it serves a variety of purposes. Use judgment at all times.

Compound privately. Results cannot always be foretold and the prescription may need to be compounded in two or three different ways before satisfactory results are obtained. It is better that the customer shall not witness these trials.

Keep the prescription, or a copy of it, before you while compounding. Never trust entirely to memory.

Compound promptly and expeditiously, but not hastily. Take pride in your skill.

Always pour from the *back* of stock-bottles and remove any drops adhering to the lip by touching with the stopper.

Use the smallest graduate that will hold the liquids.

For weighing extracts and sticky semi-solid bodies, a counter-balanced paper sprinkled lightly with lycopodium facilitates the operation.

For weighing semi-fluid bodies like ichthyol, balsam of Peru, balsam of fir, etc., a piece of parchment or waxed paper, formed into a cup by pressing over and around a cork, makes a convenient and economical receptacle. When the paper is reopened, a spatula will remove the last traces for compounding, and there is nothing to clean except the spatula.

Be neat in dispensing. The only criterion by which customers can judge of the quality of your drugs is the tastiness and care shown in dispensing. Be sure that utensils and bottles are clean, corks are whole, and that packages are wrapped neatly.

Write the label plainly and evenly. Remove any old labels, if the bottle is furnished, before pasting on a new one. If proprietary remedies are prescribed in original packages with special directions, remove the labels and substitute your own.

Never paste one label over another; neither will stick as well as when fastened to the bottle alone. Besides, it is unsafe.

Labels are easily removed after soaking in water. By fastening a piece of wet blotting paper or sponge over the label, by means of a rubber band, the soaking process can be effected while the bottle is being filled.

Flour, dextrin and tragacanth all make popular label-pastes; the last is perhaps as popular as any. Acacia makes the most adhesive mucilage, but is expensive. All need a very little oil of clove, oil of bay, cresylic acid, or other antiseptic agent, to keep them sweet.

Tragacanth paste should be made quite thin; 10 or 15 grains to an ounce of water, with about one drop of oil of clove. A more adhesive paste, which is adapted for use on tin, wood, or glass, is prepared by dissolving half an ounce of tragacanth and two ounces of acacia in half a pint of water. This is strained through cheese-cloth to render it smooth, then seven grains of thymol dissolved in two fluidounces of glycerin are added, with enough water to make a pint of paste.

Dextrin makes a very limpid mucilage, and its adhesiveness is increased by acetic acid—about quarter as much acetic acid as gum.

Flour makes the cheapest paste, but is somewhat troublesome to prepare. It must be well boiled. Rye flour, in the proportion of four ounces to a pint of water, is preferred. The addition of half an ounce of alum or a fluidrachm of nitric acid increases its adhesiveness.

An economical and thin mucilage, which is used by a number of pharmacists, is made by dissolving the residue which remains on the filter after making tincture of myrrh, in water. This residue consists almost entirely of gum, and is quite adhesive.

Special pastes for attaching labels to tin containers are,—starch 1 lb., water 10 pints, solution of tin chloride 4 oz., glycerin 1 oz., oil of sassafras 30 minims. Boil until a clear mucilage is obtained. Another paste is made by dissolving glue or gelatin in glacial acetic acid.

Butternut wood, says Mr. W. C. Durkee, makes the best surface for pasting. It absorbs the moisture quickly so that three or four dispensers can use it in common, without soiling the front of the labels. Accumulated paste on its surface is easily removed by washing with boiling water; once or twice a week being usually sufficient. Black walnut resembles it closely in appearance, but is not as good for this purpose. The board should, of course, be unvarnished.

Mr. Durkee used a sliding board, set into the counter, for pasting. An inch or two of open space over the board allows of air circulation and the drying of the board. The paste-pot is a shallow ointment-pot set into a tin receptacle in the board, and then flat brushes lie in a groove beside the pot. This makes a convenient and cleanly arrangement, and avoids litter and unsightliness.

A piece of wire stretched across the top of an ointment-pot will serve to remove superfluous paste from the brush and keep the sides of the pot clean.

Paste the label evenly on the front of the bottle, a little above the center. All bottles, even round ones, have a front. Avoid an excess of paste. To smooth the label on the bottle place a piece of clean paper over it and rub. To make labels stick on tin, coat the tin first with a thin layer of tincture of benzoin (or any resinous tincture) and let it dry; then use ordinary paste. Butter of antimony or glycerin may be used (sparingly) in place of the resinous coating, if preferred.

Poison labels, except for liniments and purely external remedies, are best omitted from prescriptions, but shake labels may be used freely whenever there is any suspicion of their need.

For a **label varnish**, collodion serves well. A varnish prepared by dissolving 300 grains of gum dammar, 114 grains of gum turpentine, and 77 grains of sandarac in enough alcohol to make 4 fluidounces, is a good varnish.

The Pharmaceutical Journal published the following formulas for a label varnish—

Copal 4 ounces, ether, acetone and alcohol, each 5 fluidounces.

White shellac $3/4$ oz., mastic, 2 oz., Venice turpentine $1/4$ oz., acetone 4 fl. oz., denatured alcohol 12 oz.

A varnished label will look better if the label is first coated with a thin solution of gelatin and allowed to dry, then the varnish applied over this. The gelatin prevents the liquid varnish penetrating the paper and making it semi-transparent and gray in place of the normal opaque-white.

Corks may be rendered absolutely impervious to ether vapor and extremely volatile liquids by soaking them in a hot 2 $1/2$ per cent solution of gelatin containing 5 per cent of glycerin, then dipping into a solution of tannic acid. Tannate of gelatin is formed in the pores of the cork, and makes it absolutely impervious. Corks so prepared also fit better.

To render corks acid-proof soak them in melted paraffin. Both the gelatin solution and the paraffin must be hot, so that they can be absorbed by the cork. Paraffined corks are usually slippery, and need to be tied in.

The most valuable "stock in trade" of the prescription pharmacist is the confidence of the public. Tact and adroitness may preserve this under difficulties. Two incidents will illustrate:

A dispenser, while wrapping the bottle, suddenly remembered that one important ingredient of that prescription had been left in the balance pan. The customer was a nervous gentleman, who had implicit confidence in the compounder. To confess the carelessness would be a blow to the customer's faith, and would result in the loss of a valuable customer. To send the bottle away without this ingredient was even worse. But the accidental (?) dropping and breaking of the bottle settled the question. An apology and a second compounding followed, the customer had no suspicion of wrong, and the medicine was properly prepared.

In a second case, the messenger had left the store with the bottle of medicine before a similar mistake was discovered. The clerk who was sent to rectify the mistake managed to overtake the messenger, and in running against him caused the bottle to be dropped and broken. After an apology and a wordy argument, the medicine was again prepared, this time free of charge.

Use only clean utensils. There is a knack in cleaning, too. For graduates, a cleansing fluid, consisting of a solution of soap in diluted ammonia water, or potassa solution, is a convenient one at the sink, but it must not be used indiscriminately. Sawdust or powdered pumice makes a desirable addition for mortars. If soap is added directly to a graduate coated with tincture of chloride of iron, or any other metallic salt solution, an insoluble soap is at once formed on the glass which is not easily removed. It is always best to first rinse the measure in running water, then any adhering matter is more easily observed, and can be removed by proper means.

Resinous matter, oils, balsams, oleo-resins, phenols, cresols, etc., are best removed by means of soap, or a cleansing fluid like the above, applied with a stiff brush.

Oleates, lead plaster, and similar metallic soaps, can be first dissolved in turpentine or kerosene, then this is removed with soap. Oil of turpentine aids in removing many odorous and sticky substances from mortars, graduates, etc.

Iodoform is removed, odor and all, by washing first with caustic potassa or soda, then rinsing with a little alcohol.

Metallic salts, if soluble, are rinsed out with water, aided, if needed, by a little nitric or hydrochloric acid. Diluted acids are best, and will sometimes be effective where strong acids fail.

Insoluble or slowly soluble salts may be decomposed by the appropriate reagent, or dissolved by another salt solution. (See table of compound solvents.) Ferrocyanide of iron, which stains mortars badly, is easily removed by caustic potassa.

Collodion and solution of gutta-percha, if undried, may be coagulated by a flow of water, a thin non-adherent film forming which is easily removed. If the film sticks, a mixture of ether and alcohol must be used for collodion, and chloroform for the gutta-percha. Goulard's solution and lime deposits are removed with weak acetic or nitric acids.

Greasy substances, ointments, etc., are easiest removed from tiles or mortars by scrubbing with sawdust. A box of sawdust kept in a handy place eases the labor of cleansing greasy utensils and containers wonderfully. The sawdust is returned to the box and used until it all is impregnated with grease, when it should be renewed.

Clean sawdust also furnishes a ready means of cleansing drug-mills, by running through the mill two or three times.

Next to sawdust soft paper is best for mortars and tiles. The last traces of grease are removed by solution of potassa, or by means of soap solution.

The quickest and easiest way to warm a mortar or tile for ointment or pill-making is to wet the inside with alcohol and set it on fire. Half a drachm of alcohol is sufficient as a rule. Do not have the pestle in the mortar while the alcohol is burning.

A methenamine tablet makes a handy substitute for an alcohol lamp or bunsen burner. A 5-grain tablet will burn for two or three minutes, giving a hot sootless flame and leaving practically no residue. This suffices to boil water in a test tube.

Shot is not the best thing for scrubbing bottles. It is composed of lead—a soft metal which easily wears away—containing a little arsenic. When shaken in a bottle streaks of lead may be left on the inside of the glass, which may act the part of an unwelcome reagent, if not otherwise objectionable. Professor Patch tells of a precipitate occurring from this cause in a mixture containing tincture of chloride of iron and diluted phosphoric acid. The traces of lead may be removed by rinsing with diluted nitric acid, but coarse sand is a better scrubbing agent. The sand is also handy to have (if clean) for use in percolating.

The best tests of cleanliness, which should always be applied to graduates and mortars, are the absence of odor, of taste in the last

rinsings, and in the case of non-odorous metallic salts, particularly poisons, the failure of a test when the appropriate reagent is applied.

For bottles or utensils to be used for hypodermic injections, distilled water should be used for final rinsing, or, in case this is scarce and expensive, water which has been filtered through a porcelain bougie, like the Pasteur or Boston filters. Water so filtered affords a good substitute for distilled water in some cases—not in all, for it still contains dissolved matter.

For the quick filtration of collyria or other solutions, an aspirator is most effective and convenient, if permanent connections are made. A small Chapman aspirator, which is readily screwed on to a water-tap by means of a reducing-coupling, connected by rubber tubing with a bell-jar carrying a small funnel, and resting upon a greased plate, makes all the connections needed. When used, a plain-folded filter is placed in the funnel, a graduate or bottle is put underneath to catch the filtrate, a flow of water from the tap operates the pump, and the liquid is forced rapidly through the filter by air-pressure, the pressure coming, of course, from exhaustion of the air inside the bell-jar.

Such an arrangement is inexpensive, always ready for use, and can be utilized, particularly the aspirator portion, for other purposes. Small filters will stand the pressure without breaking, while large ones would need some reinforcement at the apex.

Holes can be cut in glass, corks, or rubber stoppers by means of a rat-tail file. For glass, wet the file with turpentine, or, better, a solution of camphor in turpentine. For rubber stoppers, wet the file with caustic potassa solution.

Drops obtained from the end of a stopper held against the lip are commonly larger than those obtained directly from the lip. But drops are always uncertain things. Don't forget to pour or drop from the back of the bottle, and keep the front and the label clean.

Gutta-percha makes a good mending tissue. A strip of it glued upon the sides of a funnel or graduate, over the crack, will preserve its usefulness. Heat will make it adhere to the glass so that it will not come off easily, and it is not affected by weak acids or alkalis. Equal parts of gutta-percha and shellac, melted together, make the strongest kind of cement for pestle-handles or for broken mortars. It should be applied quickly, and the mortar-edges or pestle should be warm.

A rubber pad or a piece of rubber sheeting under a mortar prevents slipping and saves much effort in holding the mortar steady. It is specially useful in making pill-masses, stiff ointments and emulsions. It also reduces noise.

A cylinder of tin (made from an old vaseline or tomato can), just large enough to set over the spirit-lamp, affords a good support for vessels to be heated, and keeps the heat where it is most wanted. Holes or slits must be cut in both the top and bottom of the cylinders, to allow a circulation of air, else the lamp will not burn. The freer the circulation the better the heat.

Broken spatulas, if there is a sufficiently long stub, are easily ground or filed into shape, and are useful in pill-massing or ointment-making.

Finally, all rules have their exceptions, but exceptions should not be made the rule.

TABLE OF LATIN TERMS USED IN PRESCRIPTIONS

The more important, in heavy type, should be memorized by the student

TERM OR PHRASE	CONTRACTION	MEANING
<i>Abdomen, inis</i>	Abdom.....	The belly.
<i>Ablutio, ionis</i>		A washing, cleansing.
<i>Absente febre</i>	Abs. febr.....	In the absence of fever.
<i>Ac</i>		And, also, besides.
<i>Accurate</i>		Carefully, accurately.
<i>Accuratissime</i>	Accuratiss.....	Most carefully, most accurately.
<i>Acerbitas, atis</i>		Sourness.
<i>Acerbus, a, um</i>		Sharp, sour, harsh (to the taste).
<i>Acetum saturninum</i>		Solution of subacetate of lead.
<i>Ad (prep. w. accus.)</i>		To, up to.
<i>Ad conciliandum gustum</i>		To suit the taste.
<i>Adde, addatur</i>	Add.....	Add (thou), let it be added.
<i>Addantur, additus</i>		Let them be added, adding.
<i>Addendus, addendo</i>		Adding, for or by adding.
<i>Adde cum tritu</i>	Add. c. trit.....	Add with trituration.
<i>Additis sub finem coctionis</i>		Adding toward the end of boiling.
<i>Ad defectionem animi</i>	Ad. def. anim.....	To fainting.
<i>Ad gratam aciditatem</i>		To an agreeable sourness.
<i>Ad gratum gustum</i>		To an agreeable taste.
<i>Adhibendus</i>	Adhib.....	To be administered.
<i>Adjacens</i>		Near to.
<i>Ad libitum</i>	Ad. lib.....	At pleasure.
<i>Admove, admoveatur</i>		
<i>Admoveantur</i>	Admov.....	Apply, let it or them be applied.
<i>Admoveantur durante dolore</i>		Let it be applied when in severe pain.
<i>Ad partes dolentes</i>	Ad. part. dolent.....	To the painful (or aching) parts.
<i>Ad secundam vicem</i>	Ad. 2d vic.....	To the second time.
<i>Adsante febre</i>	Adst. febre.....	When the fever is on.
<i>Adversum</i>	Adv.....	Against.
<i>Ætas, atis</i>		Age, time of life.
<i>Aggrediente febre</i>	Aggred. febr.....	When the fever is coming on.
<i>Agita, agitetur</i>	Agit.....	Shake, stir, let it be shaken or stirred.
<i>Agitato, agitando</i>		With or by shaking, or agitation.
<i>Agita ante sumendum</i>		Shake before taking.
<i>Agita donec refrigerat</i>		Stir until it is cold.
<i>Agitando miscentur</i>		Let them be mixed by shaking.
<i>Agitato vase</i>	Agit vas.....	The vial being shaken.
<i>Albus, a, um</i>	Alb.....	White.
<i>Alcoholisatus, i</i>		Alcoholized, <i>i.e.</i> , powdered extremely fine.
<i>Aliquot</i>		Some, a few, proportionate.
<i>Alimentum, i</i>		Nutrient, nourishment.
<i>Alter, alteram</i>	Alt.....	The other, the rest.
<i>Alternis horis</i>		Every other hour.
<i>Aluta</i>		Leather.
<i>Alvo astricta (or adstricta)</i>	Alv ast.....	For confinement of the bowels (constipation).
<i>Alvus</i>		The belly, the bowels.
<i>Amphora, æ</i>		A pitcher, a jug.
<i>Amplus</i>	Amp.....	Large, ample.
<i>Ampulla</i>		A flask, ampul.
<i>Ana</i>	a a.....	Of each.
<i>Ante</i>		Before.
<i>Applica, applicetur</i>		Apply, let it be applied.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Aqua aërata</i>	Aq. aerat.....	Carbonated water.
<i>Aqua astricta</i>	Aq. ast.....	Frozen water, ice.
<i>Aqua bulliens</i>	Aq. bull.....	Boiling water.
<i>Aqua fervens</i>	Aq. ferv.....	Warm water.
<i>Aqua communis</i>	Aq. com.....	Common water.
<i>Aqua fontis</i> (fontalis or fontana)	Aq. font.....	Spring water.
<i>Aqua gelida</i>		Cold water.
<i>Aqua marina</i>	Aq. mar.....	Sea water.
<i>Aqua phagedænica</i>	Aq. phaged.....	Yellow wash.
<i>Aqua pluvialis</i>	Aq. pluv.....	Rain water.
<i>Aqua potabilis</i>		Drinkable water.
<i>Aqua saturni</i>	Aq. satur.....	Subacetate of lead water.
<i>Aqua urbis</i>	Aq. urb.....	City water.
<i>Aquila alba</i>		Calomel.
<i>Argilla, æ</i>		Clay.
<i>Artis lege</i>		By law of art, with skill.
Aut		Or.
<i>Bacca, æ</i>		Berry.
<i>Bacillum, i</i>		A bougie.
Balneum		A bath.
<i>Balneum arenæ</i>	Bal. ar.....	Sand-bath.
<i>Balneum maris</i>	Bal. mar.....	Salt (or sea) water bath.
<i>Balneum vaporis</i>	Bal. vap.....	Steam (or vapor) bath.
Bene		Well, good.
<i>Bibe, bibatur</i>		Drink, let it be drank.
<i>Biduum</i>		Two days.
Bis		Twice.
Bis in die, bis in dies, bis intra diem	Bis in d.	Twice a day.
<i>Bonus, a, um</i>		Good.
<i>Brachium</i>		An arm.
<i>Brevis</i>		Short.
<i>Bulliat, bulliant</i>	Bull.....	Let it (or them) boil.
<i>Butyrum</i>		Butter.
<i>Cæruleus, i</i>	Cærul.....	Dark blue, dark green.
Calefactus, i	Calef.	Warmed.
<i>Calido solvantur</i>		Let them be dissolved while hot.
<i>Calomelas or calomelanos</i>	Calom.....	Calomel.
<i>Calor, oris</i>	Calor.....	Heat, warmth.
Capiat	Cap.	Let the patient take.
<i>Capiat omnes cursu hodie</i>		Let the patient take all during this day.
Capiat quantum vis (or volueris)	Cap. quant. vis.	Let the patient take as much as he will.
<i>Capillus, i</i>		The hair.
Capsule, æ	Caps.	A capsule.
<i>Capsulæ amylicæ</i>		Amylaceous capsules, i. e. cachets.
<i>Caput, capitis</i>		The head, of the head.
Carbasus, i	Carbas.	Linen, lint.
<i>Caro, carnis</i>		Meat, of meat (flesh).
<i>Cataclitum, i</i>		A pillow.
<i>Cataplasma, atis</i>		A poultice.
<i>Catharticum, i</i>		A cathartic.
Caute		Cautiously.
Celeriter		Quickly, immediately.
<i>Cena (or cæna or cæna)</i>		Supper.
Ceratum, i		A wax salve.
<i>Charta</i>	Chart.....	Paper.
<i>Charta bibula</i>	Chart. Bib.....	Blotting paper.
<i>Charta cerata</i>	Chart. cerat.....	Waxed paper.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Charta densata</i>		Paste-board.
<i>Charta exploratoria</i>		Reagent or Litmus paper.
<i>Charta stannata</i>		Tinfoil.
Chartula	Chart.	A small paper.
<i>Chininum</i>	Chinin.....	Quinine.
<i>Cibus, i</i>		Food, victuals.
<i>Circitu</i>		Near, round, about.
<i>Cito</i>		Quickly.
Cito dispensetur!	Cito disp.!	Let it be dispensed quickly.
<i>Clarus, a, um</i>		Bright, clear.
<i>Clausus, a, um</i>		Closed, inclosed.
<i>Cochleare, cochleatim</i>	Coch.....	A spoonful, by spoonfuls.
Cochleare amplum, or	Coch. amp.	
magnum	Coch. mag	A tablespoonful.
<i>Cochleare medium or modicum</i>	Coch. med.	A dessertspoonful.
<i>Cochleare parvum</i>	Coch. parv.	A teaspoonful.
<i>Cocio</i>		Boiling.
<i>Cogantur</i>		Let them be combined.
Cola, coletur, colentur		Strain, let it (or them) be strained.
<i>Colatura (dat.)</i>	Colatur.....	To or of strained liquor.
<i>Collum, i</i>		The neck.
<i>Collunarium, i</i>		A nose-wash.
<i>Collutorium</i>	Collut.	A mouth-wash.
<i>Collyrium</i>	Collyr.	An eye-lotion.
<i>Coloretur</i>		Let it be colored.
<i>Commisce, commiscetur, commiscetur</i>		Mix together, let it or them be mixed together.
<i>Commode (adv.)</i>	Commod.....	Rightly, properly, suitably.
<i>Comprimata</i>		Squeezed.
<i>Concisus</i>		Cut.
<i>Concussus, i</i>		Shaken.
<i>Concute, concutiatur</i>		Shake, let it be shaken.
<i>Conditum, i, um</i>		Candied.
<i>Conditum, i</i>		A confection, comfit.
<i>Confricamentum, i</i>		A liniment for rubbing.
Congius	Cong.	A gallon.
<i>Conquassando</i>		By vigorous shaking.
<i>Conserva</i>		A conserve; also preserve.
<i>Consperge, conspergetur</i>	Consperg.....	Dust or sprinkle, let them be sprinkled or dusted.
<i>Contere, conterantur</i>	Contere.....	Rub together, let them be rubbed together.
<i>Conterendo</i>		With or by rubbing together.
<i>Continuantur remedia</i>	Cont. rem.....	Let the medicines be renewed.
Contra		Against.
<i>Contritrus, a, um</i>	Contrit.....	Broken, ground, crumbled.
<i>Contusus, a, um</i>	Contus.....	Bruised.
Coque, coquetur, coquantur	Coq.	Boil, let it (or them) be boiled.
<i>Coquantur simul</i>	Coq. simul	Boil together.
<i>Cor, cordis</i>		The heart.
<i>Cotula, æ</i>		A measure.
<i>Coxa</i>		The hip.
<i>Cras, crastinus</i>	Cras.....	To-morrow.
<i>Cras sumendus</i>		To be taken to-morrow.
<i>Cras mane</i>		To-morrow morning.
<i>Cras nocte</i>		To-morrow night.
<i>Cras vespere</i>		To-morrow evening.
Cujus, cujus libet	Cuj., cuj. lib.	Of which, of whatever you please.
Cum	c.	With.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Cum guttis aliquot</i>		With a few drops.
<i>Cursu (abl.)</i>		In the passing of, during.
<i>Cyathus</i> , or.....	Cyath.....	
<i>Cyathus vinarius</i>	Cyath. vinar.....	A wineglass.
Da, detur, dentur	Da, det., dent.	Give, let it (them) be given.
<i>De (prep. w. abl.)</i>		From, down.
<i>Deaurentur</i>		Let them be gilded.
<i>Debita spissitudinis</i>	Deb. spiss.....	Let to a proper consistence.
<i>Debitus, a, um</i>		Due, proper.
<i>Decanta</i>		Decant.
<i>Decoctum</i>	Decoc.....	A decoction.
<i>Decoque, decoquetur, decoquen-</i> <i>tur</i>		Boil down, let it be boiled down.
<i>Decubitus</i>	Decub.....	Lying down.
<i>Dedie in diem</i>	Ded. in d.....	From day to day.
<i>Dein, deinde</i>		Afterward, then.
<i>Deglutiatur (antur.)</i>		Let or may be swallowed.
<i>Dejicerit, dejiciatur</i>		Will purge, let it be purged.
<i>Dexter</i>		Right.
<i>Diebus alternis</i>	Dieb. alt.....	Every other day.
<i>Dies (diei, gen.)</i>	d.....	A day.
<i>Digere, digeretur, digerentur</i>		Digest, or let be digested.
<i>Diluculum, i, diluculo</i>		Daybreak, at dawn.
<i>Dilue, dilutus, a, um</i>		Dilute, diluted.
Dimidius, a, um	Dim.	One-half.
<i>Directiones</i>	Dir.....	Directions.
<i>Directione propria</i>	Dir. prop.....	With proper directions.
<i>Dispensa, dispensetur</i>	Disp.....	Dispense, let it be dispensed.
Divide, dividatur, dividantur ..	Divid.	Divide, let be divided.
<i>Dolor, dolore</i>		Pain, in pain.
<i>Donec</i>		Until
<i>Donec alvus dejecerit</i>		Until the bowels move.
<i>Donec alvus commode purgetur</i> ..		Until the bowels are properly purged.
<i>Donec alvus soluta fuerit</i>		Until the bowels are loosened.
<i>Donec habeas colaturæ</i>		Until you have of strained liquor.
<i>Donec leniatur dolor</i>		Until the pain is relieved (or assuaged).
<i>Donec sint residua</i>		Until there is—of residue.
Dosis		A dose.
<i>Dulcedo (idinis) dulcitas, atis</i> ..	Dulc.....	Sweetness.
<i>Duplico</i>		In duplicate.
<i>Eadem (fem.)</i>		The same.
<i>Edens, ntis</i>		Eating.
Ejusdem		Of the same.
<i>Electuarium</i>	Elect.....	An electuary.
<i>Emesis</i>		Vomiting.
<i>Emplastrum ad clavas</i>		Corn plaster.
<i>Emplastrum conglutinans</i>		Sticking plaster.
<i>Emplastrum magdaleone</i>		Plaster in rolls.
<i>Emplastrum epispasticum</i>	Emp. episp.....	} A blistering plaster.
<i>Emplastrum vesicatorium</i>	Emp. vesic.....	
<i>Emulgens, entis</i>		An emulsifying agent.
<i>Enema, enemata</i>	Enem.....	A clyster. (Injection for the rectum.)
<i>Epistomium</i>	Epistom.....	A stopper, bung.
Et		And.
<i>Etiā</i>		Also, besides.
<i>Etiā nunc</i>		Yet, also, besides.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Evanuerit</i>		Shall have passed away, disappeared.
Ex or E (w. alb.)		From, out of.
<i>E qua formentur</i>		From which are formed.
<i>E quibus sumatur</i>		From which are given.
<i>Exhibeatur</i>	Exhib	Let it be exhibited (administered).
Ex modo prescripto	E. m. p.	After the manner prescribed (as directed).
<i>Ex paululo aquæ</i>		From (or in) a very little water.
<i>Experime</i>		Try (thou).
<i>Ex parte</i>		Partly.
<i>Exprime, exprimatur</i>		Express, let it be expressed.
<i>Extende, Extendatur</i>		Spread, let it be spread.
<i>Extende super alutam</i>	Extend sup. alut	Spread upon leather.
<i>Extende super pannum</i>		Spread upon cloth.
<i>Extrahe, extrahatur</i>		Extract (thou), let it be extracted.
<i>Extractum</i>	Ext	An extract.
Fac, fit, fiat, fiant	Ft.	Make, let be made.
<i>Facere</i>		To make.
Farina		Flour, meal.
<i>Fasciculus</i>	Fascic	A little bundle.
<i>Febris</i>		Fever.
<i>Febre durante</i>		During the fever.
<i>Femoris interni</i>	Fem. inter.	To the inner thigh.
Fervens (entis)	Ferv.	Hot.
<i>Fictilis, e</i>		An earthen vessel.
Filtra	Filt.	Filter.
<i>Filtrum</i>	Filt.	A filter.
<i>Filtrum chartæ</i>		Filter paper.
Flavus, a, um	Flav.	Yellow.
<i>Fluidus, a, um</i>	Fld.	Fluid.
<i>Flores benzoës</i>		Benzoic acid.
<i>Flores cinæ</i>		Santonica.
<i>Flores zinci</i>		Oxide of zinc.
<i>Folius, i</i>	Fol.	A leaf.
<i>Fomentum, i</i>		A fomentation. Stupe.
<i>Formentur</i>	Form.	Let them be formed.
<i>Frigor, oris</i>	Frig.	Cold.
<i>Frustrillatim (adv.)</i>	Frust.	In small pieces, little bits.
<i>Fuerit</i>		Shall have been.
Fuscus a, um		Brown, dark.
<i>Gargarisma</i>	Garg.	A gargle.
<i>Gelatina</i>		Gelatin.
Globulum		A globule.
Gradatim		Gradually.
Granulum		A granule; small pill.
Granum, grana	gr.	A grain, grains.
<i>Gratus, a, um</i>		Pleasant, agreeable.
<i>Grossus, a, um</i>		Large, coarse.
<i>Gummi mimosæ</i>		Gum arabic.
Gutta, guttæ	gtt.	A drop, drops.
<i>Guttatim</i>		By drops.
<i>Harum pilularum</i>		Of these pills.
<i>Harum pulverum</i>		Of these powders.
Haustus, i	Haust.	A draught.
<i>Hebdoma, æ</i>		A week, for a week.
<i>Herba, æ</i>		An herb.
<i>Heri</i>		Yesterday.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Hora</i>		An hour.
<i>Hora decubitus</i>	Hor. dec.....	At bed-time.
<i>Horis intermediis</i>	Hor. interm.....	In the intermediate hours.
Hora somni	Hor. som.	At bed-time.
<i>Horæ unius spatii</i>		At the end of an hour.
<i>Idem</i>		The same.
<i>Identidem</i>		Repeatedly, often.
<i>Idoneus, a, um</i>		Suitable, convenient.
<i>Idoneo vehiculo</i>	Idon. vehic.....	In a suitable vehicle.
<i>Illico</i>		Then, immediately.
<i>Illico lagena obturatur</i>		Let the bottle be stoppered immediately.
<i>Immitatur, immitantur</i>		Let it (them) be introduced into, placed in.
<i>Imprimis</i>		Chiefly, first.
In		In, within, upon—(sometimes) not.
<i>Incide, incisus</i>		Cut, cutting.
<i>Inde</i>		Therefrom.
<i>Indies</i>		Daily.
<i>Infunde</i>		Put or pour in.
<i>Ingere, ingerendus</i>		Put or force into, forcing into.
<i>Ingerendo capsulas gelatinosas</i>		Putting into gelatine capsules.
<i>Injiciatur</i>	Injic.....	Let it be injected.
<i>In impetu effervescentiæ</i>		In the height of effervescence.
<i>In lagena bene obturata</i>		In a well-stoppered bottle.
<i>In loco frigido</i>	In loco frig.....	In a cold place.
<i>In massam subigantur</i>		Let them be kneaded into a mass.
<i>In massam cogantur</i>		Let them be combined in a mass.
<i>In olla ferrea vitreata</i>		In a glazed iron pot.
<i>In partes æquales</i>		Into equal parts.
<i>In pulmento</i>		In gruel.
<i>Instar</i>		The form and size of.
<i>In vaso clauso</i>		In a closed (covered) vessel.
<i>In vaso leviter clauso</i>		In a loosely closed vessel.
Inter, internus		Between, inner.
<i>Involve, involvuntur</i>		Cover (coat), let them be covered.
<i>Involve gelatina</i>		Coat with gelatin.
<i>Invergantur</i>		Let them be moistened, sprinkled.
<i>Ita</i>		In such manner.
<i>Iteretur, iterentur</i>		Let it (or them) be repeated.
<i>Jam</i>		Now.
<i>Jentaculum, i</i>	Jentac.....	Breakfast.
<i>Jucunde</i>	Jucund.....	Pleasantly.
<i>Julapium</i>		A lemonade.
<i>Julepum</i>	Jul.....	A julep.
<i>Juscellum</i>		A broth.
<i>Juscullum</i>		Soup.
<i>Juxta, juxtim</i>		Near to, nigh, close by.
Kalium	K.	Potassium.
<i>Kali</i>		Potassa.
<i>Kali præparata</i>		Potassium carbonate.
Lac, lactis		Milk, of milk.
<i>Lagena, æ</i>		A bottle.
<i>Lamella, æ, lamina, æ</i>		Plate, leaf, layer, scale.
<i>Lana, æ</i>		Flannel, wool.
<i>Languor, oris</i>		Faintness, feebleness.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Lapideus, a, um</i>	Lapid.....	Of stone, stony.
<i>Lapis infernalis</i>		Silver, nitrate, lunar caustic.
<i>Largus, a, um</i>		Abundant, plentiful.
<i>Laridum, lardum</i>		Lard.
<i>Latus, a, um</i>		Broad, wide.
<i>Latus, eris (lateris)</i>		The side, of the side.
<i>Latere admoveatur</i>	Lat. admov.....	Let it be applied to the side.
<i>Lateri dolenti</i>	Lat. dol.....	To the painful side.
<i>Laxamentum ventris</i>		Purging, evacuating.
<i>Laxus, a, um</i>		Loose, open (opp. to <i>astricta</i>).
<i>Lectus, i</i>		A bed, couch.
<i>Leniter</i>		Easily, gently.
<i>Leniter terendo</i>		By rubbing gently.
<i>Leviter</i>		Lightly.
<i>Leviter clausus</i>		Lightly closed.
<i>Linctus, i</i>		A linctus or lohoch.
<i>Linimentum, i</i>		A liniment.
<i>Lintum, i</i>		Lint.
<i>Liquor, oris</i>	Liq.....	A liquor.
<i>Luteus, a, um</i>	Lut.....	Yellow, golden yellow.
<i>Macera, maceretur, maceantur</i>	Macer.....	Macerate, let it (them) be macerated.
<i>Macera, donec refrigerant</i>		Macerate until cold.
<i>Macera per horas tres</i>		Macerate three hours.
<i>Macera per sextam horæ partem</i>		Macerate ten minutes (one-sixth part of an hour).
<i>Magdaleon, ntis</i>		A roll.
<i>Magnus, a, um</i>	Magn.....	Large.
<i>Mane (indeclin.)</i>		Morning, in the morning.
<i>Mane bene, mane plane</i>		} Early in the morning.
<i>Mane primo</i>		
<i>Manipulus, i</i>		A handful (bundle).
<i>Manus, i</i>		The hand.
<i>Mare, maris</i>		The sea, of the sea, also sea-water.
<i>Massa, æ</i>	Mass.....	A mass.
<i>Matula</i>		A vessel, pot (for liquids).
<i>Matutinus, a, um</i>		In or of the morning.
<i>Medius, a, um</i>	Med.....	Midst, middle, medium.
<i>Mensura</i>		By measure.
<i>Mica, æ</i>		A crumb, morsel.
<i>Mica panis</i>	Mic. pan.....	Crumb of bread.
<i>Minimum, i</i>	m.....	A minim.
<i>Minutum, i</i>		A minute.
<i>Misce, misceatur, misceantur</i>	M.....	Mix, let it (them) be mixed.
<i>Misce accuratissime</i>	M. accur.....	Mix very intimately.
<i>Misce bene</i>	M. bene.....	Mix well.
<i>Misce caute</i>	M. caute.....	Mix cautiously.
<i>Misceatur fortiter conquassanda</i>		Let it be mixed with violent agitation.
<i>Mistura</i>	Mist.....	A mixture.
<i>Mitte, mittatur, mittantur</i>		Send, let it (them) be sent.
<i>Mitte tales</i>		Send of such, send like this.
<i>Modicus, a, um</i>		Moderate (sized), middling.
<i>Modo dictu</i>	M. dict.....	As directed (in the way said).
<i>Modo præscripto</i>	M. p.....	As directed or prescribed.
<i>Mollis, is</i>		Soft.
<i>Mora, æ</i>		A delay.
<i>More dictu</i>	Mor. dict.....	In the manner said (as directed).
<i>More solitu</i>	Mor. sol.....	In the accustomed manner.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Mortarium, i</i>	Mortar.....	A mortar.
<i>Mos, moris</i>	Mortar.....	Manner, of manner, custom, work.
Natrium, i		Sodium.
<i>Ne tradas sine nummo</i>	Ne. tr. s. n.	Do not deliver unless paid.
<i>Necnon</i>		And also, and yet.
Niger, nigra, nigrum		Black.
<i>Nihilum album</i>	Nihil. alb.	Zinc oxide.
<i>Nisi</i>		Without, unless.
<i>Non</i>		Not.
Non repetatur	Non rep.	Do not repeat.
<i>Novus, a, um</i>		New, fresh.
<i>Nox, noctis</i>		Night, of the night.
<i>Noxa, æ, or noxia, æ</i>		An injury, hurt.
<i>Nucha</i>		The nape of the neck.
<i>Numerus, i</i>		Number.
<i>Numero</i>	No.....	In number.
<i>Nunc</i>		Now.
<i>Nutricius (nutritus), a, um</i>		Nourishing, nutritious.
<i>Nutritus, us</i>		Nourishment.
<i>Nux, nucis</i>		Nut, of a nut.
<i>Obduce, obducatur</i>		Cover or conceal, let it be covered or concealed.
<i>Obducantur foliis argenti</i>		Coat (cover) with silver.
<i>Obductus, a, um</i>		Covered, concealed, coated.
<i>Obtritus, a, um</i>		Crushed.
<i>Oculus, a, um</i>		Enclosed.
Octarius	O	A pint.
<i>Octuplus, octuplo</i>	Octup.....	Eight-fold—in eight-fold.
<i>Oculus, i</i>		The eye.
<i>Odoramentum, i</i>	Odoram.....	A perfume.
<i>Odoratus, a, um</i>	Odorat.....	Odorous, smelling, perfuming.
<i>Odora, odoretur</i>		Perfume, let it be perfumed.
<i>Oleosus, a, um</i>		Oily.
<i>Oleum—sine igne</i>		Cold drawn or pressed—oil.
<i>Olla, æ</i>		A pot, jar.
<i>Ollicula, æ</i>		A little pot.
Omnis		All, every.
<i>Omni hora</i>	Omni. hor.....	Every hour.
<i>Omni mane</i>	Omni. man.....	Every morning.
<i>Omni nocte</i>	Omni. noct.....	Every night.
Optimus, a, um	Opt.	Best.
<i>Opus (indecl.)</i>		Need, necessity.
<i>Oryza</i>		Rice.
<i>Os, oris</i>		The mouth, of the mouth.
<i>Ovi putamen (inis)</i>		An egg shell.
<i>Orum, i</i>		An egg.
<i>Pabulum, i</i>		Food, nourishment.
<i>Pallidus, i</i>		Pale, pallid.
<i>Panis, i</i>		Bread.
<i>Pannus, i, pannulus, i</i>		A cloth, rag.
<i>Para, parita, paretur, paratus, i</i>		Prepare, let be prepared, prepared.
<i>Paretur inde</i>		Let be prepared therefrom.
<i>Pars, partis, parti</i>		A part, of the part, to the part.
<i>Pars affecta fricetur</i>		Let the affected parts be rubbed.
<i>Parte affecta fricetur</i>		Rub upon the affected part.
Partes æquales	P. e.	Equal parts.
<i>Partitus, a, um</i>		Divided.
<i>Partitis vicibus</i>		In divided doses.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Parvus, a, um; parvulus, a, um</i>		Little, very little, an infant.
<i>Pastillus, i</i>		A pastille, lozenge.
<i>Paucus, a, um, paucies (adv.)</i>		Little, few, seldom.
<i>Paulatim</i>		Little by little, gradually.
<i>Pectus, oris</i>		The breast.
<i>Penicillum, i, peniculus, i</i>		A pencil, brush, little roll.
<i>Per (prep. w. acc.)</i>		Through, by means of, very.
<i>Peractus, a, um</i>		Finished.
<i>Percalefactus, a, um</i>		Thoroughly heated.
<i>Percola, percoletur</i>		Strain through, percolate, let be strained through.
<i>Perge, pergetur</i>		Proceed with, continue, let be continued.
<i>Perinde</i>		In the same manner, just as.
<i>Perpurus, a, um</i>		Very clean.
<i>Pervesperi (adv.)</i>		Very late in the evening.
<i>Pes, pedis, pedi</i>		The foot, of, to, the foot.
<i>Pessarium, i, Pessulum, i</i>	Pess.	A pessary.
<i>Petroxolinum</i>	Petrox.	Petroxolin.
<i>Phiala, æ</i>	Ph.	A phial.
<i>Phiala prius agitata</i>	P. p. a.	The vial having first been shaken.
<i>Pilula, æ</i>		A pill.
<i>Pilus, i</i>		The hair.
<i>Pinguis, is</i>	Ping.	Fat, grease.
<i>Pistillum, i</i>		A pestle.
<i>Placebo</i>		I will satisfy (will please).
<i>Plasma, atis (n.)</i>		A form, figure. (Glycerite of starch.)
<i>Plasma, plasmetur</i>		Mould (thou), let it be moulded.
<i>Plenus, a, um</i>		Filled.
<i>Poculum, i, pocillum, i</i>		A drinking cup, a little cup.
<i>Pomatum, i</i>		A perfumed ointment.
<i>Pondere</i>		By weight.
<i>Pondus, eris, ponderatus, i</i>		A weight, weighing.
<i>Pondus civile</i>		Avoirdupois weight.
<i>Pondus medicinale</i>		Apothecaries' weight.
<i>Pone</i>		After, behind.
<i>Post cibo</i>	Post cib.	After eating.
<i>Postridie</i>		On the next day, the following day.
<i>Potus, us</i>		A drink, a drinking.
<i>Præ (prep. w. abl.)</i>		Before, also very.
<i>Prandium, i</i>	Prand.	Dinner.
<i>Pridie</i>		On the day before.
<i>Primus, a, um</i>		First, earliest, beginning.
<i>Prius (adv.)</i>		Before, former.
<i>Pro (adv. and prep. w. abl.)</i>		For, in favor of, before, according to.
<i>Pro dose</i>		For a dose.
<i>Proprius a, um</i>		Special, particular.
<i>Pro ratione ætatis</i>		According to the condition of age, <i>i.e.</i> , according to the age of the patient.
<i>Pro re nata</i>	P r. n.	As occasion arises, occasionally, as needed.
<i>Pro potu cathartico</i>		For a cathartic drink.
<i>Proximo</i>	Prox.	Nearest.
<i>Pugillum, i</i>	Pugil	A pinch.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Pulpa, æ</i>		Pulp.
<i>Pulvis, eris</i>	Pulv.	A powder.
<i>Pulvis grossus</i>	Pulv. gros.	A coarse powder.
<i>Pulvis subtilis</i> or.....		
<i>Pulvis subtilissimus</i>	Pulv. subtil.	A smooth (very smooth) powder.
<i>Pulvis tenuis</i> or.....		
<i>Pulvis tenuissimus</i>	Pulv. tenu.	An extremely fine (attenuated) powder.
<i>Purgativis, i</i>	Purg.	A cathartic, purging.
<i>Purus, a, um</i>	Pur.	Pure, clean.
<i>Pyxis, idis</i>		A small box, a pill box.
<i>Quadrans, antis</i>		A fourth, quarter.
<i>Quadrum, i</i>		Square.
<i>Quadruplo</i>		In four-fold, quadruple.
<i>Quam (adv.)</i>		As much as, in what manner.
<i>Quam libet</i>		
<i>Quam (or qua) (vis, volueris)</i>	q. v.	As much as you wish.
<i>Quantum libet</i>	q. l.	
<i>Quantum placet</i>	q. p.	As much as you please.
<i>Quantum vis or volueris</i>	q. v.	
<i>Quantum sufficit</i>		
<i>Quantum satis</i>	q s.	A sufficient quantity.
<i>Quaqua hora</i>		Every hour.
<i>Quaque, quisque</i>	q. q.	Each, every.
<i>Quartus, i</i>		Fourth.
<i>Quibus</i>		To or from which.
<i>Qui libet</i>		Any, whatever you please.
<i>Quisquam or quisquis</i>		Anything.
<i>Quoque</i>	q. q.	Also.
<i>Quorum</i>		Of which.
<i>Quotidie</i>		Daily.
<i>Quoties</i>		As often as.
<i>Quoties requiritur</i>		As often as is required.
<i>Rarus, a, um</i>		Loose, thin, rare.
<i>Ratio, onis</i>		Relation, proportion, condition.
<i>Recens, ntis</i>	Rec.	Fresh, recent, newly.
<i>Recipe</i>	R.	Take (thou). A recipe.
<i>Redactus, i</i>	Redact.	Reduced.
<i>Redactus in pulverem</i>	Red in pulv.	Reduced to powder.
<i>Regio, onis</i>		Region, direction, portion.
<i>Relectus, a, um</i>		Opened, loosened.
<i>Reliquus, i</i>	Reliq.	Remaining, the remainder.
<i>Renova, renovetur</i>		Renew, let it be renewed.
<i>Renovetur semel</i>	Renov. semel	Let it be renewed once only.
<i>Repetatur, repetantur</i>	Rept.	Let it (or them) be repeated.
<i>Res, rei</i>		A thing, object, substance, affair.
<i>Residuus, a, um</i>		Residual, remaining.
<i>Retineatur</i>		Let it be withheld.
<i>Rictus, us</i>		Wide open, distended.
<i>Rigidus, a, um</i>		Rigid hard, inflexible.
<i>Rotula, æ</i>		Globules.
<i>Ruber, rubra, rubrum</i>	Rub.	Red, ruddy.
<i>Rudicula, æ</i>		A spatula.
<i>Rudis, is</i>		A stirring rod.
<i>Rumen, imis</i>		The throat.
<i>Saccellatio, onis</i>		A sack, a dry poultice.
<i>Sacculus, i</i>		A medicated sack—a pad.
<i>Saccharum saturni</i>		Acetate (sugar) of lead.
<i>Sæpis, sæpe</i>		Often, frequently.
<i>Sal, salis</i>	Sal.	Salt, also shrewdness.
<i>Sal amarum</i>		Magnesium sulphate.
<i>Sal mirabile</i>		Sodium sulphate.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Saltem</i>		At least.
<i>Sanguis (inis), sanguineus</i>		Blood, bloody.
<i>Saponamentum, i</i>		An opodeldoc.
<i>Sapor, is</i>		A flavor, delicacy.
<i>Satis, is</i>		Enough, sufficient.
<i>Scapula, arum</i>		The shoulder blades.
<i>Scatula, æ</i>	Scat.	A box.
<i>Scrupulus, i</i>	Scr. or S.	A scruple
<i>Scutum, scuto</i>		Protection, for protection.
<i>Scuto pectori</i>		For protection to the breast.
<i>Secundo</i>		Secondly, in order.
Secundum artem	s. a.	According to art.
Secundum legem	s. l.	According to law.
<i>Semel</i>		Once, a single time.
<i>Semi, semis</i>	ss.	A half, half.
<i>Semihora</i>		Half hour.
<i>Sensim</i>		Gently, gradually, slowly.
<i>Seorsum</i>		Sundered, apart, separate.
<i>Separatim</i>	Separ.	Separately.
<i>Septimana</i>		A week.
<i>Sericum, i</i>		Silk.
<i>Sericum adhaesivum</i>		Silk court-plaster.
<i>Sericum oleatum</i>		Oiled silk.
<i>Sero</i>		Late, at a late hour.
<i>Sesuncia</i>		An ounce and a half.
Sesqui		Once and a half.
<i>Sesquihora</i>		An hour and a half.
<i>Sevum, i</i>		Suet, tallow.
<i>Sextans (ntis), sextus</i>		Sixth-part, sixth.
<i>Si</i>		If.
<i>Sic</i>		So, in this manner, thus.
<i>Sicca, Siccetur</i>		Dry, let it be dried, or drained.
<i>Siccus</i>		Dry, dried.
Signa, signetur	Sig.	Mark, imprint (thou). Let it be imprinted.
<i>Signanter</i>		Clearly, distinctly.
<i>Sile hujus</i>		Keep (thou) silence concerning this!
<i>Simplex, simplicis</i>	Simp.	Simple, unmixed.
Simul		Together.
<i>Sinapismus, i</i>		A mustard poultice, sinapism.
Sine		Without.
<i>Sine expressione</i>	S. expr.	Without expressing, pressing.
<i>Singillatim, singularis</i>		One by one, singly.
<i>Singulorum</i>	Sing.	Of each.
<i>Si non valeat</i>	Si. n. val.	If it does not answer—be of value.
Si opus sit	Si. op. sit.	If it is best—needed.
<i>Si vires permittebant</i>	Si. vir. perm.	If the strength will permit.
<i>Sit</i>		Let it be.
<i>Sit in promptu</i>		Let it be in readiness.
<i>Sitis (is), siti</i>		Thirst, for thirst.
<i>Solatium, ii</i>		Soothing, assuaging.
<i>Solutus, a, um</i>		Accustomed, ordinary.
<i>Solus</i>		Alone, only.
Solve, solvatur	Solv.	Dissolve, let it be dissolved.
Solutus, solutio, onis	Sol. or solut.	Dissolved, solution.
<i>Solutio tandem</i>		To or in the solution finally.
<i>Solve cum leni calore</i>		Dissolve with a little heat.
<i>Somnus</i>		Sleep.
<i>Sparadrapus, i</i>		A spread plaster.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Spiritus vini rectificatus</i>	S. V. R.	Alcohol.
<i>Spiritus vini tenuis</i>	S. V. T.	Proof spirit.
<i>Spissitudo, inis</i>		Thickness, consistency.
<i>Spissus, a, um</i>	Spiss.....	Dense, hard.
<i>Statim</i>		Immediately, at once.
<i>Steatina, æ</i>		Salve mulls, steatins.
<i>Stet, stent</i>		Let it or them stand.
<i>Stibium, i</i>		Antimony.
<i>Stillatim</i>		By drops, in small quantities.
<i>Stilus</i>		A stake, crayon.
<i>Stomachus, i</i>		The stomach, alimentary canal, gullet.
<i>Stratum, i</i>		Layer, stratum.
<i>Suavis</i>		Pleasant, agreeable.
Sub		Under, somewhat.
<i>Subactus</i>		Subdued, sinking.
<i>Sub finem coctionis</i>		Toward the end of boiling.
<i>Subigatur, subigantur</i>		Let it (them) be subdued, overcome.
<i>Subinde</i>		Frequently.
<i>Subtilis</i>		Fine, smooth, nice.
<i>Succus, i</i>		Juice, sap.
<i>Suggillationi</i>		To the bruise.
Sume, sumat, sumantur, sumatur, sumendus	Sum.	Take or employ, or consume. Let him take, let it be taken, to be taken.
<i>Sumat talem</i>	Sum. talem.....	Let the patient take—like this.
<i>Summo mane sumendus</i>		To be taken very early in the morning.
<i>Summus, a, um</i>		Highest, summit.
Super		Above, upon, over.
<i>Superbibe</i>		Drink afterward.
<i>Suppositoria, æ</i>	Suppos.	A suppository.
<i>Suppositoria rectales</i>	Suppos. rect.	Rectal suppositories.
<i>Suppositoria urethrales</i>	Suppos. ureth.	Urethral suppositories.
<i>Syrupus fuscus</i>		Brown syrup, i.e., molasses.
<i>Tabella, æ</i>	Tab.....	A tablet, lozenge.
Talis, is		Of such, like this.
<i>Tam</i>		So far, in so far.
<i>Tandem</i>		At last, finally.
<i>Tantum, i</i>		So much, so many.
<i>Tegmen, or tegumen, inis</i>		A cover.
<i>Tempus, oris</i>		Time.
<i>Tenuis</i>		Fine, weak, thin.
<i>Tepidus, a, um</i>		Tepid, lukewarm.
Ter		Thrice, three times.
<i>Ter in die</i>	t. i. d.	Three times a day.
<i>Tere, teretur</i>		Rub, triturate. Let it be rubbed.
<i>Teres, etis</i>		Rubbed, smooth, polished.
<i>Tere simul</i>	Ter. sim.	Rub (triturate) together.
<i>Testa, æ</i>		A shell.
<i>Testa ovi</i>		An egg shell.
<i>Thion, thionas, atis</i>		Sulphur, sulphate.
<i>Tinctura thebarica</i>		Laudanum, tincture of opium.
<i>Triplico</i>	Trip.....	Triplicate.
<i>Tritura, trituretur</i>	Trit.	Triturate, let it be triturated.
<i>Trochiscus</i>	Troch.....	Troche, lozenge.
<i>Tum</i>		Then, next, furthermore.
<i>Turbidus, a, um</i>		Turbid, muddy, not clear.
<i>Tussis, is</i>		A cough.

TERM OR PHRASE	CONTRACTION	MEANING
<i>Tuto</i>		Safely.
<i>Ubi</i>		Where, wherever, whenever.
<i>Una, æ</i>		The arm, or elbow.
Ultima, ultima	Ult.	Lastly, at the last.
<i>Ultimo præscriptus</i>	<i>Ult. præsc.</i>	The last ordered.
<i>Una</i>		To one, together.
Uncia, æ		An ounce.
<i>Unctulus, a, um, unctus, a, um</i>		Besmeared, anointed.
<i>Unctus, us</i>		An anointing, anointment.
<i>Unguentum, i</i>	<i>Ung.</i>	Ointment, unguent.
<i>Unguilla, æ</i>		An ointment-box.
<i>Urgens, entis</i>		Pressing, urgent.
Ustus, a, um		Burned.
<i>Usurpandus</i>		To be used.
<i>Usurpeter</i>		Let it be used.
<i>Usus, us</i>		Use.
<i>Utendus, a, um</i>		To be used.
<i>Ut or uti</i>		That, so that, in order that.
Ut dictum	Ut dict.	As directed.
<i>Utere, utendus, i</i>		Make use of, to be used.
<i>Utendus more solito</i>	<i>Utend. mor. sol.</i>	To be used in the usual manner.
<i>Vapor, oris</i>		Steam, vapor.
<i>Vas, vasis</i>		A vessel, utensil, bottle.
<i>Vas vitreum</i>	<i>Vas. vit.</i>	A glass vessel.
<i>Vehiculum, i</i>	<i>Vehic.</i>	A vehicle.
Vel (or ve as a suffix)		Or.
<i>Venenosus, a, um, venenum, i</i>		Poisonous, a poison.
Verus, a, um		True, real, genuine.
<i>Vesper, eris</i>		The evening.
<i>Vesperma, æ</i>		Supper.
<i>Vicis, is, vices</i>		Change, alteration, turns.
Viridis, is, viride, is		Green.
<i>Vis, viris</i>		Strength, vigor, life.
<i>Vitreus, a, um</i>		Of glass, glazed.
<i>Vitrum, i</i>		Glass.
Volatilis, is, volatile	Volat.	Volatile.
<i>Vomito, onis, vomitus, us</i>		Vomiting.

NUMERALS

CARDINALS

<i>Unus</i>	One.
<i>Duo</i>	Two.
<i>Tres</i>	Three.
<i>Quatuor</i>	Four.
<i>Quinque</i>	Five.
<i>Sex</i>	Six.
<i>Septem</i>	Seven.
<i>Octo</i>	Eight.
<i>Novem</i>	Nine.
<i>Decem</i>	Ten.
<i>Undecim</i>	Eleven.
<i>Duodecim</i>	Twelve.
<i>Tredecim</i>	Thirteen.
<i>Quatuordecim</i>	Fourteen.
<i>Quindecim</i>	Fifteen.
<i>Sexdecim</i>	Sixteen.
<i>Septemdecim</i>	Seventeen.
<i>Octodecim or duo de viginti</i>	Eighteen.
<i>Novemdecim or un de viginti</i>	Nineteen.
<i>Viginti</i>	Twenty.
<i>Viginti unus or unus et viginti</i> }	Twenty-one.
<i>Triginta</i>	Thirty.
<i>Quadraginta</i>	Forty.
<i>Quinquaginta</i>	Fifty.
<i>Sexaginta</i>	Sixty.
<i>Septuaginta</i>	Seventy.
<i>Octoginta</i>	Eighty.
<i>Nonaginta</i>	Ninety.
<i>Centum</i>	One hundred.

ORDINALS

<i>Primus</i>	First.
<i>Secundus</i>	Second.
<i>Tertius</i>	Third.
<i>Quartus</i>	Fourth.
<i>Quintus</i>	Fifth.
<i>Sextus</i>	Sixth.
<i>Septimus</i>	Seventh.
<i>Octavus</i>	Eighth.
<i>Nonus</i>	Ninth.
<i>Decimus</i>	Tenth.
<i>Undecimus</i>	Eleventh.
<i>Duodecimus</i>	Twelfth.
<i>Tertius decimus</i>	Thirteenth.
<i>Quartus decimus</i>	Fourteenth.
<i>Quintus decimus</i>	Fifteenth.
<i>Sextus decimus</i>	Sixteenth.
<i>Septimus decimus</i>	Seventeenth.
<i>Octavus decimus</i>	Eighteenth.
<i>Nonus decimus</i>	Nineteenth.
<i>Vicesimus</i>	Twentieth.
<i>Vicesimus primus</i>	Twenty-first.
<i>Tricesimus</i>	Thirtieth.
<i>Quadragesimus</i>	Fortieth.
<i>Quinquagesimus</i>	Fiftieth.
<i>Sexagesimus</i>	Sixtieth.
<i>Septuagesimus</i>	Seventieth.
<i>Octogesimus</i>	Eightieth.
<i>Nonagesimus</i>	Ninetieth.
<i>Centesimus</i>	Hundredth.

CHAPTER III

NOMENCLATURE

The temptation to physicians to abbreviate in writing prescriptions makes it necessary that the pharmacist should be thoroughly conversant with chemical nomenclature, particularly in regard to those bodies which are most frequently prescribed as remedies.

A salt or chemical may be known by several names—its trade or common name, its Latin or scientific name, and in many cases also by a technical or descriptive name.

The common or trade name may have been derived from the names of those who first brought them into notice, as Glauber's or Signette's salt, or from the place from which they were first obtained, as Epsom or Rochelle salt. The Latin or scientific names designate, in a general way, the chemical composition of the bodies, and when there are a number of salts or bodies which contain the same elements, but in different proportions, more definitely descriptive names may be applied to them to avoid confusion.

Thus, "chloride of mercury" may mean either calomel or corrosive sublimate, but the terms *mild* chloride of mercury and *corrosive* chloride of mercury, *protochloride* of mercury and *bichloride* of mercury are definite, and cannot be confused.

The first of these terms gives a general idea of the salt—composed of mercury and chlorine; the second distinguishes between the medicinal and physical action of two chlorides which exist, one being "mild," and the other "corrosive;" the third of the terms also distinguishes between the two chlorides, one being the "proto" (first or lowest) chloride, and the other the "bi" (second or higher) chloride.

Unfortunately, no one system of nomenclature is satisfactory for all, and much confusion may arise unless the dispenser understands the principles which underlie each system. A single body may have several trade-names, and the Latin title may be thought too long.

The third term attaches certain prefixes or suffixes to the negative (acid) term, which have a constant meaning, and thus distinguish the salt clearly from others of a similar composition. This method may be used for all definite chemical compounds, but if carried out in some cases, ridiculously long words would result, and thus it is not always practical, although very convenient in many cases.

The prefixes and terminations in general use are as follows:

PREFIXES

Mono (Gr. *monos*, one). **Proto** (Gr. *protos*, first).

These are employed to designate a single atom or molecule of acid radical in combination with a base, or the first or lowest number of a series, when more than one proportionate combination is known.

Before the names of radicals beginning with a vowel, the final *o* of these is generally omitted, for the sake of euphony.

Examples.— PbO , Lead monoxide. FeO , Iron monoxide, or protoxide. FeCl_2 , iron protochloride (*not monochloride*).

Sesqui (Lat. *sesqui*, one and a half), meaning three atoms or molecules of acid radical to two of basic (since chemistry does not admit of splitting atoms), the ratio being one to one and a half.

Examples.— Fe_2O_3 , Iron sesquioxide (FeCl_3 is sometimes called sesquichloride—the chloride of the sesquioxide). Al_2O_3 , Aluminum sesquioxide.

Bi, or **Bin** (Lat. *Bis*, twice), **Di** (Gr. *dis*, twice), **Deuto** (Gr. *deuteros*, second), meaning two, or double, where two molecules of acid radical are combined, or twice as many molecules as there are of the basic radical. **Di** has also been used to refer to the basic in a similar way.

Examples.— HgI_2 , Mercury biniodide, or deutoiodide. CS_2 , Carbon disulphide, $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2$ ($\text{C}_2\text{H}_3\text{O}_2$)₂ Lead diacetate.

Ter (Lat. *ter*, three). **Tri** (Gr. *tria*, three). Three atoms, or molecules of the basic radical.

Examples.— AuCl_3 , Gold terchloride. Fe_2O_3 , Iron trioxide. As_2O_3 Arsenic trioxide. $\text{Fe}_2(\text{SO}_4)_3$, Iron tersulphate.

Quadra (Lat. *quattuor*, or *quadras*, four). **Tetra** (Gr. *tetratos*, fourth), meaning four atoms, or molecules, of acid radical.

Examples.— SnCl_4 , Tetra, or quadrachloride, of tin. PtCl_4 , Tetra-chloride of platinum.

Penta (Gr. *penta*, five). **Quinque** (Lat. *quinque*, five), meaning five.

Example.— PCl_5 , Phosphorus pentachloride.

Hexa (Gr. *hexa*, six). **Sext** (Lat. *sex*, six), meaning six.

Example.— SI_6 , Sulphur hexaiodide.

Hepta (Gr. *hepta*, seven). **Sept** (Lat. *septem*, seven), meaning seven.

Example.— Cl_2O_7 , Chlorine heptoxide.

Poly (Gr. *pollos*, or *polu*, many), meaning many equivalents—usually when the exact formula is in doubt, as poly-iodides, many atoms (above three) of iodine combined with a base, etc.

Sub (Lat. *sub*, under). **Hypo** (Gr. *hupo*, under, or Lat. *hypo*, after). **Sub** refers to the base, and is used to designate salts which are composed of an oxide and another acid radical in varying proportions, or the so-called basic salts. Thus *subacetate* of lead is a combination of lead oxide PbO and lead acetate $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2$. *Subsulphate* of iron is an oxy- or basic sulphate, approximating $\text{Fe}_3\text{O}(\text{SO}_4)_2 + \text{Fe}_2(\text{SO}_4)_3 = \text{Fe}_4\text{O}(\text{SO}_4)_5$. Bismuth *subnitrate* $\text{Bi}(\text{OH})_2\text{NO}_3$ (approximately). Most of these salts vary in composition, hence their formulas are not included in the Pharmacopœia.

The term *hypo* refers to the acid radical, and usually indicates the lowest of a series of oxyacid salts.

Examples.— KClO , Potassium hypochlorite.

KH_2PO_2 , Potassium hypophosphite.

Per (Lat. *per*, above). **Hyper** (Gr. *hyper*, above). **Super** (Lat. *super*, above). The contracted form *per* is mostly used, and indicates the highest of a series of compounds, as contrasted with *sub* and *hypo*.

It is used mostly with oxy acids; when it refers to those containing the largest number of atoms of oxygen, the culmination of a series.

Examples.— KClO_4 , Perchlorate of potassium. H_2O_2 , Peroxide of hydrogen. FeCl_3 , Perchloride of iron.

Ortho (Gr. *orthos*, straight). Used to distinguish substances in a normal condition from a modified form of the same, or from others which have been derived from them by heat or other causes.

Examples.— H_3PO_4 , Orthophosphoric acid.

Pyro (Gr. *pur*, fire). Used to designate that the body has been produced by heat (fire). Thus $2\text{H}_3\text{PO}_4$, or $\text{H}_6\text{P}_2\text{O}_8$ + heat becomes $\text{H}_4\text{P}_2\text{O}_7$, pyrophosphoric acid, water (H_2O) being driven out.

$\text{C}_7\text{H}_6\text{O}_5$ gallic acid, heated becomes $\text{C}_6\text{H}_6\text{O}_3$ pyrogallic acid, CO_2 being driven out.

Meta (Gr. *meta*, beyond). Used to designate an altered condition, as distinguished from the ortho and pyro (and para) forms.

Thus, $\text{H}_4\text{P}_2\text{O}_7$ + heat becomes 2HPO_3 , metaphosphoric acid, water being driven out.

(The terms ortho, pyro and meta, as applied to *inorganic* compounds usually distinguish between forms produced by heat or similar causes.)

Para (Gr. *para*, from beside, near to, about, etc.). Used with *organic* compounds, when three bodies having the same chemical composition, but differing in physical properties (solubility, melting and boiling points, etc.) and certain chemical and medicinal properties, are to be distinguished. Such cases are differentiated by the terms ortho, meta and para.

Examples.— $\text{C}_6\text{H}_4(\text{OH})_2$, Ortho-dihydroxy-benzol or pyrocatechin.

$\text{C}_6\text{H}_4(\text{OH})_2$, Meta-dihydroxy-benzol or resorcin.

$\text{C}_6\text{H}_4(\text{OH})_2$, Para-dihydroxy-benzol or hydrochinon.

Para also designates molecular aggregations of certain organic compounds, as $\text{C}_2\text{H}_4\text{O}$ —aldehyde and $(\text{C}_2\text{H}_4\text{O})_3$ or $\text{C}_6\text{H}_{12}\text{O}_3$ paraldehyde.

Hydro (Gr. *hudor*, water), used to designate the binary acids, *i. e.*, those composed of only two elements, the prefix referring then to the hydrogen, as HCl , hydrochloric acid, H_2S , hydrosulphuric acid.

An (Lat. *an*, without). **De** (Lat. *de*, away from) meaning without or deprived of. Used to denote something which has been removed, therefore implying that the removed substance usually exists in the body normally.

Examples.—Anhydrous, without water (or moisture).

Deodorized, deprived of odor.

TERMINATIONS

Ide, Id,¹ Uret.—Terminations used with salts composed of a base united to a *single element* or with *cyanogen*, as an acid radical, the latter being used mostly with sulphur, phosphorus and cyanogen.

Examples.— KI , Potassium iodid(e).

K_2S , Potassium sulphid(e), or sulphuret, sulfid.

KCN , Potassium cyanid(e), or cyanuret.

H_2S , Sulphuretted hydrogen, or hydrogen sulphid(e).

H_4P , Phosphuretted hydrogen.

¹ The latest nomenclature prefers the termination *id*, and also substitutes *f* for *ph* in many cases, as sulfur, etc.

Ous, Ite.—When a series of acids differ only in the proportion of oxygen which they contain, the lower members of the series end in *ous* and the salts of these in *ite*.

Ic, Ate.—The highest members of such series of acids, or those which contain the most oxygen, end in *ic*, and the salts of these in *ate*.

Examples.— H_2SO_3 , Sulphurous acid, K_2SO_3 potassium sulphite.

H_2SO_4 , Sulphuric acid, K_2SO_4 potassium sulphate.

The following series well illustrates the use of some of these prefixes and terminations:

HCl , *Hydro-chlor-ic* acid. KCl , Potassium chloride, or hydrochlorate.

HClO , *Hypo-chlor-ous* acid. KClO , Potassium *hypo-chlor-ite*.

HClO_2 , *Chlor-ous* acid. KClO_2 , Potassium chlor-*ite*.

HClO_3 , *Chlor-ic* acid. KClO_3 , Potassium chlor-*ate*.

HClO_4 , *Per-chlor-ic* acid. KClO_4 , Potassium *per-chlor-ate*.

Oid (Gr. *eidos*, resemblance), used to express similarity in character and properties (not in composition).

Examples.—Alkaloid, resembles an alkali.

Crystalloid, resembles a crystal.

Resinoid, resembles a resin.

Ine, In.—In the Pharmacopœia these terminations are used to distinguish between alkaloids and other proximate principles. All alkaloids end in *ine*; Latin, *ina*; while glucosides, neutral principles, etc. end in *in*; Latin, *inum*.

Examples.—Morphine. Latin, Morphin*a*.

Quinine. Latin, Quinin*a*.

Picrotoxin. Latin, Picrotoxinum.

Santonin. Latin, Santonin*um*.

CHAPTER IV

MIXTURES

Draught (Lat. *Haustus-us* or *Potus-us*), a mixture which is intended to be swallowed at a single dose. It usually measures from two to twelve fluid-ounces.

Drops (Lat. *Gutta-æ*), a term applied usually to stimulating or carminative mixtures, which are given in small doses and diluted when taken.

Linctus (Lat. *Linctus-i*), a thick and viscid liquid, composed of honey, syrup, etc., with medicinal matter, intended to be licked from a spoon. Also called a **lochoch**. It is adapted particularly for throat and bronchial tubes, coughs, etc.

Liniment (Lat. *Linimentum-i*), a liquid or very soft solid, usually of an oily or irritant character, used externally for the purpose of producing local action. They are applied mostly by rubbing, and when fluid are specifically called **embrocations** (Lat. *embrocatio-onis*); or they may be applied with a brush, and are then called **paints**. Lat. *Pigmentum-i*, also *Littus-oris*. In the latter case they are usually anodyne in action.

Lotion (Lat. *Lotio-onis*), an aqueous solution or mixture, for local application, usually without rubbing. They are usually aqueous fluids, are less powerful than liniments, and are applied in various ways. When used for specific purposes they have special names.

Injection (Lat. *Injectio-onis*), a lotion which is injected into the passages of the body by means of a syringe. When injected into the rectum it is called an **enema** (Lat. *enema-atís*), or **clyster**, and is used warm. Its purpose may be for producing evacuation of the bowels, for local medication, or (rarely) for general nutrition or medication. It is generally of a soapy or mucilaginous nature.

Collunarium is a nostril injection.

Gargle (Lat. *Gargarisma-atís*) is a wash or lotion for the throat.

Collyrium (Lat. *Collyrium-i*) is a wash for the eyes; an eye-water.

Spray (Lat. *Nebula-æ*), a lotion or oily solution applied by means of an atomizer.

Inhalation, or Vapor (Lat. *Vapor-oris*), a fluid containing volatile medicine, which is either heated or added to boiling water, and the steam which arises is inhaled in order to obtain action on the throat or air-passages; or they are used in a special apparatus so arranged that air is drawn through the strong solution, and, becoming saturated with the medicines, in vapor, is drawn into the lungs through the mouth or nostrils.

Bath (Lat. *Balneum-ei*), a lotion or solution intended to be added to water for general application.

In general, the term "mixture" indicates all liquid preparations consisting of two or more simple bodies, or galenical preparations, intended for internal administration.

U. S. P. MIXTURES.—In the U. S. Pharmacopœia and National Formulary the term "mixture" (*Mistura*) is restricted to liquid preparations containing finely divided solid matter in partial suspension. Thus, in the official sense a mixture is always a cloudy or muddy liquid, while in the general use of the term a mixture may be either clear or cloudy.

The art of preparing mixtures may in some cases be very simple, while in others it is very complex. The range of medicines which are

prescribed in this form is very wide, embracing all chemical bodies, powdered drugs and galenical preparations.

But not only because the variety of mixtures which are called for is almost inexhaustible, but because these bodies are **brought together in the condition most conducive to changes**, is the art of combining bodies to form the best mixture, the most difficult to acquire. A prescription calling for the simplest form of mixture may be followed by one which requires much study and skill for its proper compounding.

Many bodies which may safely be combined in the solid form cannot be brought together in the presence of liquids without undergoing change.

Thus, subnitrate of bismuth and bicarbonate of sodium may be mixed and dispensed in powders without change, but when shaken with water they react slowly, and each is partially decomposed, carbonic acid gas being liberated and the stopper blown out by its pressure.

Chemical changes, then, may take place in mixtures which would not occur were the same bodies combined in a dry form.

A complete classification of mixtures is quite impossible, but a partial classification may be made, which will include the greater portion of these preparations.

SIMPLE SOLUTIONS

A solution has been defined as the blending together of the molecules of two bodies to form a clear liquid.

If we place a lump of sugar in water, it immediately begins to disappear, and after a few moments none of it can be seen, and the liquid will be perfectly clear. If we use the same amount of sugar in a fine condition (granulated), the disappearance is more rapid, and if the liquid be agitated it is still more so.

If we use hot water in place of cold, the sugar disappears almost immediately.

Thus, **solution is hastened** by having the solid in a fine condition, still more rapid if the liquid and solid be agitated together, and most rapid of all (with few exceptions) when the solvent is hot.

If, however, we drop sugar into chloroform or benzine, or many other liquids, it will not disappear, even if the liquid be warmed and agitated, but will remain in the condition in which it was placed in the liquid. Sugar therefore dissolves in water, but not in chloroform or benzine.

The solution which is formed will always measure more than the liquid which is used to make it, but not as much as the sum of its constituents; that is, not as much as the bulk of the original liquid plus the bulk of the original solid.

Thus, an ounce of sugar dissolved in an ounce of water will make more than a fluidounce of solution, but less than two fluidounces. For this reason, prescriptions often call for an amount of solvent or diluent sufficient to make the mixture measure up to a definite amount, the exact amount not being specified, because the room which the solids will occupy when dissolved cannot be calculated, but must be ascertained by experiment.

The same principle applies to two liquids as to a solid and a liquid.

If we add alcohol to water a clear homogeneous liquid results, which *measures less* than the sum of the quantities of each taken, showing that alcohol is soluble in water. If we use phenol in place of the alcohol a portion of the phenol will disappear or dissolve, but the remainder will separate and float upon the surface of the water.

If we heat the water and phenol to about 200° F. (or 85° C.) they will then mix to form a clear homogeneous liquid in all proportions, showing that phenol is only partially soluble in cold water, but freely soluble in hot water. Again, if we shake together chloroform and water, or some oil and water, each mixture will separate into layers showing no apparent change in the volume of either liquid, because oil and chloroform are practically insoluble in water or water in them.

Again, if we rub together camphor and chloral, or camphor and thymol, a clear liquid results, which is probably a solution of one solid in the other.

In the case of two liquids or two solids either body may be considered the solvent, as when ether and water are shaken together the water dissolves 8 per cent of ether and the ether dissolves 2 per cent of water. In the case of a liquid and a solid the liquid is considered the solvent and the solid the body dissolved.

Most bodies, whether solid, liquid, or gaseous, can be dissolved in some liquid, but none are soluble in all liquids. Some are capable of forming very strong solutions and in a brief time, while others dissolve slowly and only in small proportions.

In some cases a body which is only slightly soluble is yet quickly soluble, as cream of tartar. In all cases the rapidity with which the solution is formed as well as the amount of body dissolved is dependent upon the temperature. When all of a body is dissolved that is capable of dissolving at that temperature the solution is called *saturated*, but a solution which is saturated at one temperature will be either *super-saturated* or *subsaturated* at all other temperatures.

In pharmacy the temperature which is best adapted to saturated solutions is 20° C. (68° F.) because the temperature of living-rooms where solutions are supposed to be kept or used is rarely below this point, and at all higher temperatures the solutions (with a few exceptions) will be subsaturated.

When no other liquid is designated for a solution, water is understood. Besides this, other important solvents are alcohol, mixtures of alcohol and water, glycerin, oils, ether, chloroform, benzine, etc.

The solubility of each body in the different liquids can be learned by reference to each in the text or reference books.

There is no general rule for solubility, but in case a body is in question the chemical nature of which is understood, but no reference to its solubility in any given liquid can be found, a judgment as to the probability of such a solution can be made according to the law given by Prof. Ostwald, viz.: that "solubility is determined to some extent by the *chemical analogies* both of the substance dissolved and the solvent." Thus, almost all monatomic alcohols are soluble in common alcohol, and all organic acids in acetic acid. The alcohols and organic acids all contain the group (*HO*) in their formulas, and are generally soluble in water (H_2O), the solubility decreasing as the proportions of carbon in the compounds increase. Thus we have benzol, C_6H_6 ,

insoluble in water, but phenol, C_6H_5HO , is soluble to the extent of 5 per cent (cold), hydroquinol, $C_6H_4(HO)_2$, is much more soluble, while pyrogallol, $C_6H_3(HO)_3$, is very soluble.

Here the larger the proportion of the radical HO the more freely will the body dissolve in water (H_2O), while similar compounds which contain no HO are insoluble.

Nearly all mixtures contain a solution or a mixture of solutions, and thus these occupy a very important position in dispensing. Many liquids dispensed as a mixture consist of a solution of a salt in an aqueous fluid, either alone or mixed with other fluids or flavoring.

When the salt is very soluble and the solution will not be concentrated, the solvent may be placed in the bottle and the solid dropped into it.

A little shaking usually effects solution, and the other ingredients, if any, are then added.

If the salt is slowly soluble, or the solution is to be very strong, the salt should be triturated in a mortar with successive portions of the solvent until it is all dissolved, or hot water should be used.

Gums and colloidal bodies are best dissolved, after breaking into very small pieces, by circulatory displacement. In all cases the solids should be added to the liquid, not *vice versa*.

When two or more liquids of different character are prescribed with a solid, the solid should first be dissolved in the liquid which is the best solvent for it, then this solution mixed with the other liquids. In this way a clear or homogeneous mixture is most quickly obtained.

Solids will dissolve more readily when in a granular or powdered form. The granular form is to be preferred in many cases, because salts are generally more uniform in the crystalline than in the powdered condition, particularly such as contain water of crystallization. The powders are more liable to lose some of the water, and so are less soluble.

An exception to the powdered condition is found in the scale-salts of iron (citrate, soluble phosphate, etc.), which "gum up" if triturated with water, and are most readily dissolved by shaking with warm (not too hot) water.

A mixture should never be allowed to leave the dispensing counter with undissolved crystals in the bottle.

Heating a solvent to facilitate solution is not always desirable, because (1) the solvent may be injured, as in the case of the aromatic water or hydroalcoholic liquids; or (2) the subsequent admixture of an alcoholic or aromatic body to the hot liquid may volatilize some of these ingredients; or (3) a supersaturated solution may be unwittingly prepared, which will afterward recrystallize; (4) or the salt may be partially decomposed, as in the cases of chloral, bicarbonates, etc.

The dispenser must aim, not only to get a solid in solution, but also to keep it dissolved. This, of course, cannot always be accomplished where a physical or chemical incompatibility afterward ensues.

Mixtures of liquids which form a clear liquid, may be considered as solutions of one liquid in another. Even where the fluids will form a clear mixture in any order of mixing, a definite order may be desirable.

When powerful liquids in small quantities are prescribed in a mixture, such as hydrocyanic acid, solutions of arsenic, strychnine, morphine, etc., a portion of the other ingredients should be first placed in the bottle, then the powerful ingredients carefully measured, added, and the graduate rinsed with the remaining ingredient of the mixture.

In the same way, when a viscid liquid is to be mixed with a limpid one, the graduate in which the viscid liquid has been measured should be rinsed with the limpid liquid.

In case of an incompatibility, however, these considerations are of minor importance compared with that of avoiding precipitation, or change in the mixture, as much as possible.

It is very convenient, when certain salts are being frequently called for in mixtures, to keep on hand a concentrated solution of these salts. Thus strong solutions of potassium acetate, or iodide, adjusted so that one fluidrachm of the mixture will contain 15 or 30 grains of the salt, may save time in dispensing solutions.

In a few stores potassium acetate is never purchased, but a solution of the above strength made when needed by treating potassium bicarbonate with acetic acid; thus 3920 grains (8 troy ounces and 80 grains) of potassium bicarbonate dropped slowly into 12 fluidounces of acetic acid (36 per cent), and when effervescence has ceased, enough more acetic acid is added to render the liquid neutral, and then the whole carefully diluted with water to measure just one pint; one fluidounce of this solution will contain four drachms (240 grains) of potassium acetate. Where solutions of this kind are used they should be carefully measured, both when making and dispensing them, since an error in quantity is much more easily made in measure than in weight. Solutions of salts which are disagreeable to handle, as ammonium valerianate, or of salts which dissolve very slowly, as mercuric chloride (also used in very small weights), are convenient for stock-solution.

Stock-solutions are easily made by circulatory displacement. A conical percolator is tightly stoppered and filled with the solvent, then the salt is tied in a piece of thin cloth and suspended just beneath the surface of the liquid, and the percolator covered. Solution begins immediately and continues until the liquid is saturated or the salt entirely dissolved. A wide-mouth bottle may be substituted for the percolator if desired.

Where an air-blast can be used, a quick and convenient method of making large quantities of solutions is to place the salt and solvent in a bottle or jar and blow air through the liquid which agitates both the salt and the solvent and the former quickly passes into solution. If an aspirator is at hand the same result may be obtained by passing a tube through the stopper of the bottle to near the bottom, then the air is sucked through this tube and the liquid by means of a second tube which passes through the stopper, but does not touch the liquid, the other end of this being connected with the aspirator. A bit of cotton should be placed in the end of the air-tube to filter the air ere it enters the liquid. If the water has also previously been sterilized by boiling, the solution will be less liable to change or to develop fungous growths.

Among the salts suitable for stock solutions are ammonium chloride (1 in 4), magnesium sulphate (1 in 2) sodium sulphate (1 in 4), potassium bromide (1 in 2), potassium acetate (1 in 2).

Iodides, tartrates and alkaloids (salts of) are not suitable for stock-solutions unless used up promptly, because the salts quickly decompose when in solution. Most organic bodies are subject to change in this condition and thus the stock-solutions are restricted properly to solutions of metallic nitrates, sulphates, chlorides, and bromides.

Even these solutions will keep better if filtered when first made, for no matter how clear they may look at first, filtration will usually brighten their appearance, and also remove any minute particles which may encourage crystallization.

Petroleum solutions, used as sprays, have come into use in recent years. These are usually solutions of volatile oils, camphoraceous bodies (thymol, menthol, camphor, etc.), and other antiseptics in liquid petrolatum. When the bodies directed are soluble in the liquid petrolatum, these are made in the same way as aqueous solutions, but without heat. If the solids which are to be dissolved themselves liquefy when mixed, (making a eutectic mixture) a better spray is secured by dissolving them separately in the oil, rather than by just mixing the solids and dissolving the liquefied mixture in the oil. Unfortunately, however, liquid petrolatum is very limited in its solvent powers, and substances are frequently ordered which will not dissolve in the oil. In many cases, these are soluble in almond or olive oil, and a clear solution can be made by dissolving first in one of these oils and mixing this solution with liquid petrolatum. In this way a clear, oily solution can be dispensed, which is suitable for use in an atomizer. When substances are ordered which are not soluble in oils, there is no way of securing a preparation suitable for use in an atomizer unless an aqueous solution is acceptable.

COMPOUND SOLUTIONS

The term compound solution is usually applied to one containing two or more substances in solution. This use of the term would restrict the term simple solution to one substance dissolved in a liquid. But in a pharmaceutical sense the term compound solution may be applied to the dissolving of a solid which alone is insoluble in water in a solution of another salt. Thus mercuric iodide is insoluble in water but is soluble in an aqueous solution of potassium iodide, hence the latter is often used in order to make an aqueous solution of the first. This principle applies frequently in prescription practice, and in this chapter the term compound solutions is applied particularly to those in which one substance (whether solid or liquid) is used to dissolve another.

In many instances a chemical change takes place, a new salt or a double salt being formed which is soluble. In other cases, a salt may be added to prevent precipitation, on the same principle.

Quinine sulphate is only slightly soluble in water, but dissolves freely if a little acid be added to the water, being changed into an acid salt; the bisulphate, for instance, when sulphuric acid is used.

These solutions are often more stable than a solution of the principal salt, as well as being stronger; as in the case of corrosive sublimate dissolved in ammonium chloride solution. The ordinary

solution of corrosive sublimate in water is gradually decomposed, but one containing ammonium and sodium chlorides is not only more easily prepared, but is also permanent.

The following formula for a solution of corrosive sublimate (1 to 1000) for antiseptic purposes has recently been recommended, making a solution which will keep indefinitely; corrosive, sublimate, 1 Gm.; ammonium chloride, 20 Gm.; sodium chloride, 10 Gm.; distilled water, 1000 cc.

A knowledge of the best solvent for each salt or chemical is often useful to the pharmacist in manufacturing or dispensing, and may often rectify a faulty prescription. Many physicians depend upon the pharmacist to make such additions to their prescriptions as shall make them more elegant in appearance or taste, yet not alter their medicinal properties.

Thus iodine is sometimes directed in aqueous solution, and the pharmacist expected to add a sufficient quantity of potassium iodide to effect solution. Sometimes the addition of a solvent becomes a necessity; as where red iodide of mercury is prescribed in an aqueous mixture. This is insoluble in water, and is a powerful poison, safely taken only in very small doses.

To suspend it in a mixture would not be safe, because it settles very quickly; but the addition of a little potassium iodide will dissolve it, and the solution will remain evenly diffused throughout the mixture, rendering it safe as well as more elegant.

Glycerin has valuable solvent properties in many cases, and being without any decided therapeutic action the pharmacist is usually justified in using it to improve prescriptions. It is particularly valuable in solutions containing tannin, being used in many official tinctures and fluid extracts for this purpose, as well as for a partial substitute for alcohol, which it resembles in solvent properties.

It dissolves most deliquescent salts, some metallic nitrates, chlorides and sulphates, many organic acids (as tannic and gallic acids, etc.), and several metallic oxides, notably oxide of lead (litharge), which it dissolves in large quantities. It is owing to this that a mixture of glycerin and litharge makes a tenacious cement for joining porcelain, glass or wedgewood-ware, for filling the handles of pestles, etc. A high temperature greatly increases the solvent power of glycerin.

Sodium citrate, the neutral tartrates, and ammonium chloride possess remarkable solvent powers over many metallic salts. Sodium citrate entirely prevents the precipitation of iron salts in neutral solutions, and alkaline tartrates (as Rochelle salt, potassium tartrate), dissolve iron and copper hydroxides, the insoluble salts of zinc, bismuth, manganese, nickel, cobalt, chromium, and aluminum; while a boiling solution dissolves barium, strontium, magnesium, and calcium salts, also.

Advantage may be taken of these salts in preventing precipitation, when a smaller quantity will suffice than would be needed to dissolve a salt already precipitated.

The quantity of solvent salt necessary to use in various cases depends, not only upon the character of the salts involved, but often upon the strength of solution desired. For instance, one part of potassium iodide, dissolved in two parts of water, will dissolve two

parts of iodine: but if this solution be diluted with water, a portion of the iodine will be precipitated, and a further addition of potassium iodide becomes necessary.

The value of salt-solutions as solvents is recognized in the Pharmacopœia and National Formulary in the scale-salts of iron, in Fowler's, Valangin's, Goulard's and Lugol's solutions, in syrup of lime, and many others.

The following list and table offers many hints for cleansing chemical and pharmaceutical apparatus, for making solutions for use in the arts and for general prescription-knowledge.

The insoluble salts of **Benzoic Acid** are readily soluble in aqueous solutions of sodium acetate, lead acetate, or sodium nitrate; potassium nitrate, however, will not dissolve them.

Borates are more soluble in solutions of boric acid.

Carbonates are all soluble in solutions of carbonic acid, pressure being sometimes necessary in order to obtain a sufficient quantity of the gas in solution. The carbonates are by this means converted into bicarbonates, hence it may be said that all bicarbonates are soluble.

Citrates are, many of them, soluble in solutions of sodium, potassium or ammonium citrate.

Ferricyanides and **Ferrocyanides** are soluble in caustic alkalies, both fixed and volatile.

Lactates are much more readily dissolved by boiling than by cold water.

Oleates are soluble in kerosene oil, oil of turpentine and ether.

Phosphates are soluble in phosphoric acid and alkaline phosphates, and

Pyrophosphates are soluble in alkaline pyrophosphates.

Tartrates are soluble in tartaric acid and caustic alkalies.

Aqueous solutions of phenol, benzoates, salicylates, succinates and a considerable number of salts of other aromatic acids have the property of dissolving bodies which are normally only slightly soluble in water, such as volatile oils, camphoraceous substances, alkaloids, albumins, edestin, lecithin and even milk fat. This property is termed **hydrotropism** and the substance acting as the solvent is called the **hydrotropic substance**. These substances may render albumin non-coagulable by heat, and they liquefy gelatin. Drugs like acetanilid, antipyrin, phenacetin, sulphonal, anæsthesin, salipyrin, pyramidon etc. are rendered more soluble. The cause of such action is not always clear. In some cases double salts are formed; in others probably not.

TABLE OF COMPOUND SOLVENTS

Bodies slightly soluble in water, but more soluble in non-alcoholic solutions of other bodies.

SALT	SOLVENT (Salt in Aqueous Solution)
Acid Acetylsalicylic.....	Sodium Citrate (4 to 1).
Acid Arsenous.....	Weak Acids and Alkalies, Glycerin.
“ Benzoic.....	Sodium Benzoate, Sodium Phosphate, Sodium Sulphate.
“ Boric.....	Borax, Glycerin, Syrup.
“ Gallic.....	Potassium Citrate.
“ Salicylic.....	Borax and Soluble Acetates, Citrates and Phosphates.
Barium Sulphate.....	Ammonium Nitrate, Alkaline Citrates.
Bismuth Citrate.....	Ammonia Water, Alkalies.
“ Subcarbonate.....	Ammonium Carbonate.
“ Subgallate.....	Caustic Alkali Solutions.
“ Tartrate.....	Alkali Tartrates.
Borax.....	Sugar (increases the solubility).
Bromine.....	Hydrobromic Acid, Potassium Bromide, etc.
Caffeine.....	Organic Acids, Sodium Benzoate and Salicylate.
Calcium Carbonate.....	Carbonic Acid Water, Ammonium Chloride.
“ Hydroxide.....	Sugar.
“ Phosphate.....	Acids, Ammonium Chloride.
“ Sulphate.....	Nitric and Hydrochloric Acids, Potassium Nitrate, Sodium Thiosulphate, Ammonium Salts.
Cerium Oxalate.....	Ammonium Chloride.
Chrysarobin.....	Alkalies.
Cotton and Cellulose.....	Ammonio-sulphate of Copper.
Iodine.....	Potassium Iodide, other Soluble Iodides, Tannic Acid.
Iron Subcarbonate.....	Carbonic Acid Water, Sugar.
“ Ferrocyanide.....	Oxalic Acid, Alkalies.
“ Oxalate.....	Oxalic Acid and other acids.
“ Oxide and Hydroxide.....	Sugar and Citrates.
“ Phosphate.....	
“ Pyrophosphate.....	Alkaline Citrates and Tartrates.
“ Tartrate.....	
Lead Iodide.....	Ammonium Chloride, Potassium Iodide and Acetate, Sodium Thiosulphate, Alkali Solutions.
“ Oxide.....	Lead and Alkaline Acetates.
“ Sulphate.....	Ammonium Acetate.
Lithium Benzoate.....	Sodium Benzoate.
“ Carbonate.....	Carbonic Acid Water.
Magnesium Carbonate.....	Carbonic Acid Water.
“ Phosphate.....	Inorganic Acids.
Mercury Benzoate.....	Sodium Chloride, Ammonium Chloride.
“ Bichloride.....	Ammonium Chloride, Sodium Chloride.
“ Biniodide.....	Potassium Iodide, Mercury Bichloride, Sodium Thiosulphate.
“ Sulphate.....	Potassium Sulphate.
“ Ammoniated.....	Ammonium Acetate, Carbonate or Nitrate.
Phenol.....	Hot Water, Glycerin, Soap, Sodium Acetate and Valerate, Ammonium Benzoate, Salicylate, etc.
Potassium Bitartrate.....	Borax and Alkalies.
Quinine Sulphate ¹	Weak Acids, Tinct. Chloride Iron, Huxham's Tincture.
Saccharin.....	Alkalies.
Salophen.....	Caustic Alkali.
Silver Cyanide.....	Potassium Cyanide, Sodium Thiosulphate, Ammonia.
“ Iodide.....	Potassium Cyanide, Alkali Iodides.
Tragacanth (Bassorin).....	Hydrogen Peroxide.
Zinc Carbonate.....	Ammonia Water.
“ Oxide.....	Ammonium Carbonate.

¹ When quinine sulphate is ordered in solution, no acid or other solvent being designated, weak sulphuric acid should be used on account of the resulting fluorescence which is not present in other acid solutions.

Solutions of tar oil in soap—the soap being largely in excess—will give a clear solution with water in all proportions, while solutions of soap in tar oil, the oil being in excess, form emulsions with water. Pure phenol at 20° is miscible in any proportion with a saturated (at 15°) solution of sodium acetate, or with a 50 per cent solution of sodium valerate. Solutions of phenol in the latter can afterward be diluted with water without becoming cloudy or opaque. Sodium valerate solution also dissolves cresol in all proportions. Rosin soap also possesses the property of dissolving large quantities of phenol, while cresol dissolves readily in a 15 per cent solution of oleic soap, one part of the latter being capable of rendering soluble in water five times the amount of cresol. This fact explains the possibility of preparing soluble mixtures containing 50 per cent of cresol. The salicylates, benzoates, etc., of ammonium also dissolve phenol and cresol but not to the extent of soap solutions. Solutions of phenol in soap also have the property of dissolving benzine, toluene, oil of turpentine, etc.

Oil solutions, used as sprays, have become popular of late in the treatment of throat and nose diseases. Liquid petrolatum is the usual vehicle for these, and its solvent powers are more limited than the vegetable oils. Most oil-soluble substances are more soluble in olive or expressed almond oil than in petroleum oils, and some, as resorcin, aristol, iodoform, etc., are soluble in the former, but not in the latter. Since sprays must be clear and perfect solutions, the use of a vegetable oil in place of a portion of the petroleum oil is often necessary. For instance, when resorcin is directed in these oil solutions, the only method by which a clear oil solution can be obtained is to dissolve the resorcin in as little olive or almond oil as possible and mix this with the liquid petrolatum. Menthol, thymol, etc., which are soluble in the liquid petrolatum, need no special consideration except that a better preparation is usually secured when they are dissolved separately or in succession than when they are first mixed together and liquefied and the liquid dissolved in the oil. If alkaloids are directed in such solutions, the free alkaloid must be used, not the salt. Some of the free alkaloids, as cocaine, are soluble in the liquid petrolatum. Those that are not must first be dissolved in a little oleic acid, and this in turn in the petroleum oil.

PERCENTAGE SOLUTIONS

Percentage solutions or solutions containing a required percentage of active ingredients are sometimes ordered by the physician. Since percentage means the number of parts in a hundred, the only difficulty in this class of preparations should be in allowing for the contraction in making the solution.

Thus a **4 per cent solution** of cocaine hydrochloride would mean, technically, a solution containing four parts of the cocaine in every hundred parts of solution, and to make an ounce of such solution we first calculate the amount of cocaine to use, viz.: 4 per cent of 456 grains (the weight of a fluidounce of water), or 18 $\frac{1}{4}$ grains, and dissolve this amount in 438 grains (*not one fluidounce*) of water.

This will give *slightly less than a fluidounce* of solution, but the deficiency in a solution as weak as this will be scarcely observable.

If however a strong solution be desired, as a 25 per cent solution of a salt, then a larger quantity must be calculated for, because if we take 25 per cent of 456, which is 114, and use only 342 grains of water ($456 - 114 = 342$) to dissolve this amount, we shall fall considerably short of the required amount, though we should make a 25 per cent solution.

The exact amount by weight which we should have to make in order to get a fluidounce, could only be ascertained by knowing the specific gravity of such a solution and multiplying the weight of an equal volume of water by this specific gravity in order to get the weight of the required volume of solution.

This is scarcely necessary in practice, since a little judgment will enable one to choose the nearest *round number* which is likely to yield the full volume of solution. The nearest round number to 456 is 500, and calculating 500 grains to the fluidounce we would require 125 grains of the salt and 375 grains of water, still too small a quantity of water. The next round number is 600 and 25 per cent of this is 150, leaving 450 grains of water in which to dissolve it, or almost exactly a fluidounce of water, and we may expect with these quantities (viz.: 150 grains of salt and 450 grains of water) a *little more* than a fluidounce of solution, since the salt will increase the bulk somewhat when dissolved.

The excess of bulk may be dispensed (as percentage solutions are almost always prescribed alone) or thrown away as may seem best. **If another solvent than water be used**, we must also make a correction for the specific gravity of the liquid and first calculate the weight of the required volume of that liquid.

Thus if ether be used (sp. gr. 0.75), we find that a fluidounce of it will weigh $456 \times 0.75 = 372$ grs., if glycerin (sp. gr. 1.25), a fluidounce will weigh $456 \times 1.25 = 579$ grains, or if chloroform (sp. gr. 1.50), a fluidounce will weigh $456 \times 1.50 = 683$ grains.

Then these products (or their near round numbers if a strong solution is to be made) are to be taken as the basis of calculation.

In the United States, however, **percentage solutions are not always made by weight**. It is much easier for the physician in certain cases to calculate the dose if in making the solution the *solids are weighed and liquids are measured*.

In the case of aqueous solutions this makes little difference, being only a little less accurate, but with other solvents it alters the proportions of solid solvent very appreciably.

Thus a 10 per cent solution of iodoform in ether would, in the first case, contain 10 grams of iodoform in 100 *grams* of solution—about 125 cubic centimeters—while in the second case it would contain 10 grams in 100 *cubic centimeters* of solution (about 70 grams), the second method (weighing the solid and measuring the liquid) making a much stronger solution than the first.

On the other hand, if chloroform be used as a solvent, the solution would be weaker; if the chloroform be measured for making it by weight we would have 10 grams in 100 grams, about 63 cubic centimeters, while in the second case it would contain 10 grams in 100 cubic centimeters.

The tendency in the Pharmacopœia and National Formulary is toward weight-volume solutions rather than weight-weight. Weight-volume solutions, containing a definite weight in 100 volumes are more easily prepared, and since the doses are by volume the amount of substance in a dose is more accurately regulated.

Since the physician measures all liquids in dosing, a teaspoonful of solution will contain the same weight of solid whichever solvent is used (the solid being weighed and the liquid measured in making the solution), the bulk being the same in all cases, though the weight and percentage strength varies.

Again, by this rule, strong solutions are stated as much stronger than when stated in weight percentage. For instance, if we dissolve a Troy ounce of potassium iodide in 5 1/2 fluidrachms of water, we shall have just a fluidounce of solution, of which one minim would contain one grain of the iodide,—making a 100 per cent solution weight-volume though such a percentage is impossible by weight.

It is thus sometimes uncertain just what a physician wishes when he orders a percentage solution.

The object of the dispenser should always be to supply what the physician desires, but physicians differ in their objects in writing for percentage solutions, sometimes desiring them to be made by weight and sometimes by volume, and it is not always possible to tell from the reading of the prescription which the physician desires. This lack of uniformity is shown in the fact that in the two leading hospitals in Boston, each having a large corps of physicians, one corps desires all percentage solutions to be made by weight and the other by weighing the solid and measuring the liquid.

Professor Oldberg gives a simple formula for making percentage solutions by weight while measuring the water. Let a represent the number of grains of solvent, and b the percentage strength of the solution to be made. Then

$$\frac{a \times B}{100 - B} = c.$$

c represents the number of grains of salt required to add to a . For instance, to make an ounce of a 5 per cent solution.

$$\frac{455.7 \times 5}{100 - 5} = 23.981 \text{ grs.}$$

Then dissolve 24 grains of the substance in a fluidounce of water to obtain a 5 per cent solution.

On the basis of the above, Mr. H. C. Landenbeck has worked out the following table:

4.557 grs. in 1 fluidounce = 1 per cent.	0.456 grs. in 1 fluidounce = 1 in 1000.
9.289 " 1 " = 2 "	0.912 " 1 " = 1 in 500.
14.078 " 1 " = 3 "	1.141 " 1 " = 1 in 400.
18.966 " 1 " = 4 "	1.522 " 1 " = 1 in 300.
23.957 " 1 " = 5 "	2.290 " 1 " = 1 in 200.
50.576 " 1 " = 10 "	4.557 " 1 " = 1 in 100.
80.327 " 1 " = 15 "	9.289 " 1 " = 1 in 50.
113.797 " 1 " = 20 "	18.966 " 1 " = 1 in 25.
151.730 " 1 " = 25 "	50.576 " 1 " = 1 in 10.
303.460 " 1 " = 40 "	113.797 " 1 " = 1 in 5.

GASEOUS SOLUTIONS

Nearly all gases are soluble in water to a considerable extent, nitrogen being an exception—almost insoluble in water, though some of the compounds of nitrogen, as ammonia gas, NH_3 , are freely soluble.

Cold water dissolves much more gas than warm, and the amount of gas which will remain in solution is directly proportionate to the pressure. Thus one volume of water will dissolve an equal volume of carbonic acid gas under normal conditions, but if the pressure is doubled the same amount of water will dissolve two volumes of gas.

Solution of gases under pressure are not often prepared by the pharmacist, since they require special apparatus (with a few exceptions). Familiar examples of such solutions are the aerated table- and mineral-waters usually sold in bottles, and the "soda water" which is stored under pressure in metallic tanks and drawn from the "fountains" as required for immediate consumption.

All of these solutions effervesce as soon as the pressure is withdrawn, and a portion of the gas escapes.

Solutions of gas under normal pressure are often prescribed, and *should be always freshly prepared.*

In writing for these the physician usually prescribes an acid and a carbonate or bicarbonate in the same mixture and leaves it to the intelligence of the dispenser to know that the bicarbonate will be decomposed and to furnish a solution of the gas.

These solutions will always be acid to litmus paper unless an excess of the carbonate is used, because the gas is acid. They are best made in a bottle, and should never be filtered or strained. If a bright and clear solution is desired, the acid and alkaline [or saline] solutions may each be filtered before mixing, but never after the gas has been liberated. If the solution is to contain other volatile or viscid ingredients (syrops, mucliage, etc.), these should be added last, since the former will be partially lost in the effervescence, and the latter retards the escape of gas so much that the effervescence becomes tedious, or else takes place spasmodically and is liable to spurt out some of the liquid. When the quantities of acid or salt are left to the judgment of the dispenser, they should be calculated stoichiometrically.

The use of carbonic acid gas as an adjuvant to saline solutions is steadily increasing. Its value lies partly in its cooling and mildly stimulating action upon the stomach and fauces, and also in its efficiency in correcting or disguising the taste of salts, or in preventing oxidation of some easily-changed bodies.

Mixtures may contain it in solution under normal or increased pressure, in the latter case more of the gas being retained in solution.

These pressure solutions, of which effervescing solution of magnesium citrate, U. S. P., is a type, are always contained in stout, round bottles which should not be too full.

Flat-sided bottles, even when made of heavy glass, are liable to burst under the pressure, hence even the bottoms of bottles intended for this use are rounded to make them more resistant to the pressure.

A little air space in the bottle also allows for a slight increase or decrease of pressure caused by varying temperatures, with less risk of an explosion.

In making these solutions the carbonate or bicarbonate is added last, either in crystals which are not allowed to dissolve before inserting and tying in the stopper, or in a solution which is poured slowly down the side of the bottle so as to form a separate layer of liquid, as recommended by Professor E. L. Patch. In the latter case more time is allowed for inserting the stopper and less gas is lost.

Bottles containing effervescent liquids are best kept stored upon their sides, in order to keep the cork wetted and swollen, and prevent the gradual escape of gas.

Solutions containing the gas under normal pressure should be so made as to retain as much of the gas as possible. To this end the water should be *cold* (because cold water dissolves more gas than warm water), and the effervescence should take place in presence of *all* the liquid, the mixture then being bottled as soon as effervescence has ceased. Under these circumstances the liquid will dissolve about its own bulk of carbonic acid. No special bottles are required for these mixtures.

Prescriptions calling for salicylic acid, sodium bicarbonate and water are a very common type of this class. When made they are essentially a solution of sodium salicylate, saturated (under normal pressure) with carbonic acid gas, the latter being one object sought by the physician.

Chlorine solutions obtained by the action of hydrochloric acid upon a chlorate are often prescribed for affections of the throat.

In ordering a mixture containing these two bodies, the physician may wish either an acidulated solution of potassium chlorate, in which no chlorine gas is liberated or he may wish a solution containing the full amount of chlorine in solution.

In the first case the chlorate is first dissolved in the water and the acid added last, while in the second case the dry chlorate is covered with the strong acid and the reaction allowed to proceed until the bottle is filled with the chlorine fumes, the water being then added in portions, so as to check the reaction as little as possible, yet dissolve the gas before it escapes from the bottle.

When a solution of the gas is desired the method directed by the N. F. for Compound Chlorine Solution is the best.

Mixtures which by reaction give off nitric oxide gas (NO) are sometimes met with. These differ from the other gaseous reactions in that the *nitric oxide should not be retained* in the solution. The gas is liberated from nitrates or nitrites and is not only irritating, but is an active chemical agent, and may cause further change in other ingredients.

Thus, in mixtures containing spirit of nitrous ether, an acid or acid salt, and potassium or sodium iodide, there will be a reaction between the acid, nitrous ether and the iodide, free iodine and nitric oxide being liberated.



And if there be an excess of iodide present, the nitric oxide, in presence of air, will decompose this also and liberate all the iodine, hence the reaction should be allowed to take place in an open, and

preferably shallow vessel, in the presence of as little liquid as possible, so that the gas may all pass off into the air.

In all cases where a nitrate or nitrite is decomposed and liberates nitric oxide, this method of procedure should be resorted to, since a solution of the gas is never desirable for medicinal purposes.

Where the other ingredients are not injured thereby, a little heat may be resorted to, in order to remove the last portions of the gas.

MIXTURES CONTAINING INSOLUBLE BODIES

These are of two classes: Those in which an insoluble powder is *added* to the liquid, and those in which the insoluble body is *formed* in the liquid by the interaction of two of the ingredients.

In the first case, the mixture, of course, should never be filtered; in the latter case it is often a question whether filtration is proper or not. When in doubt, **DON'T**.

Mixtures of the first class are usually made by triturating the dry powder with a small portion of liquid, until a smooth paste is obtained; then this may be transferred to the bottle, and the mortar rinsed with fresh portions of liquid; or the liquid may all be mixed in the mortar, and afterward transferred to a bottle.

In some cases—where the powder is somewhat soluble in the liquid, as in case of quinine sulphate, cream of tartar, magnesium carbonate, etc.—the powder may be evenly diffused by adding to the liquid in the bottle and shaking vigorously, but in most cases trituration in a mortar is necessary to prevent lumping.

If a powdered drug, as rhubarb, for instance, be added to a liquid in a bottle, the occluded air on the surface of the powder will prevent the liquid from wetting it evenly, and lumps will form, which cannot be broken by agitation, nor be easily brought under the pestle in the presence of a large proportion of liquid, if afterward transferred to a mortar. A proper start in mixtures of this sort often saves much time. Some highly electrical powders as sulphur, quinine (alkaloid) etc. are not easily wetted by water but are helped by a trace (and only a trace) of oil. Sulphur lotions are often troublesome in this regard, making unsightly mixtures. A little powdered orris root or a minute drop of oil mixed first with the sulphur will make a much more satisfactory mixture.

Very light powders, as powdered charcoal, vegetable drugs, salol, etc., are difficult to incorporate with liquids because of their tendency to fly out of the mortar. A small amount of liquid added to these requires much trituration to uniformly moisten the powder, during which the powder flies persistently out. If too much liquid be added, the powder floats upon its surface, and cannot easily be wetted. Such powders are best treated by first making into a soft cream with glycerin or syrup, with which they can easily be incorporated, this cream being afterward triturated with the diluent, and a homogeneous mixture thus obtained. Mucilage of acacia is even better for salol and water-repellent substances.

Many salts such as subnitrate of bismuth, phosphate of calcium, magnesium hydroxide, etc. **are somewhat gelatinous when freshly precipitated**, but become hard and granular, or heavy, when dried.

These **freshly precipitated salts are of special advantage** in mixtures of this class, because they do not settle as quickly. These are beyond the range of ordinary single prescription dispensing, but can be prepared in quantities to advantage.

Milk of Magnesia is a familiar example of these, made by precipitating a solution of magnesium sulphate with sodium or potassium hydroxide, washing this precipitate by decantation until free from sulphate, then suspending in water. It corresponds essentially to calcined magnesia, but remains suspended in the water for a long time. The *Ferri Hydroxidum cum Magnesii Oxido* of the Pharmacopœia (arsenical antidote) is another illustration of these, and also of the special therapeutic value of such mixtures. A dried ferric hydroxide would not be effective as an antidote to arsenic.

Another advantage in a suspended body is that its taste is not as pronounced as when it is in solution. This is the case with quinine sulphate; when it is suspended in a liquid its bitterness is not very objectionable, but if it be dissolved by an acid, the bitterness is very pronounced. For this reason, *quinine should not be dissolved by addition of an acid unless ordered by the physician.*

Mixtures of Resinous Tinctures with Water.—Under the name of *Lac Virginis* (see page 75) a milky mixture of tincture of benzoin with rose water has long been popular for external use. If the tincture of benzoin is poured into the water in the usual way, it is precipitated in a mass and the preparation is not satisfactory. To secure a smooth, milky mixture the benzoin must be precipitated in a very fine condition. This is accomplished by either adding the tincture in a very fine stream, with constant shaking, or by adding it drop by drop with shaking. The object is to get the benzoin mixed with the whole of the water instantly, so that the resinous bodies are not coagulated but remain diffused. If the tincture touches the side of the bottle or mortar before it has diffused through the water, it tends to coagulate. But if dropped into the center of the liquid and immediately diffused it makes a milky mixture. A very fine stream forced into the water accomplishes the same purpose. This can be performed by using a pipette with a very fine orifice, letting the tincture flow into the water while the latter is being stirred vigorously, as in a graduate with a glass rod. In the absence of the pipette the tincture should be dropped slowly into the water while the latter is being stirred.

Tinctures of myrrh, of guaiac or other resinous tinctures should be handled in this way.

MIXTURES CONTAINING CHEMICALLY INCOMPATIBLE BODIES

The **greater diffusibility of undried or freshly precipitated salts** often leads the physician to prescribe in such a way that the insoluble body will be *formed in compounding the prescription* by the admixture of solutions of two incompatible salts or other bodies.

These mixtures are based on the general **law of incompatibility**, viz.: when two salts can, by interchange of their radicals, form an insoluble salt, the insoluble salt will be formed and precipitated.

Such mixtures, containing an intentional incompatibility should of course, never be filtered, but dispensed with a shake-label.

In all mixtures which are liable to form an insoluble body by reaction, **the first effort of the dispenser should be to avoid this formation if possible.** This may often be done by diluting the antagonistic bodies before mixing, or by the intervention of some viscid body, as syrup or glycerin, which may retard if not entirely prevent the reaction. The body which is liable to be precipitated should be treated much as a general prepares a weak force to meet the attack of a strong one—viz.: the weak force is first protected by fortifications and placed in such a position as to receive the attacking party in sections and not all at once.

The following prescription—a striking example of incompatibility overcome by skill in mixing—will serve to illustrate this:

R. Tinet. ferri chloridi.....	℥ii.
Spiritus ætheris nitrosi.....	℥iv.
Mucilaginis acaciæ.....	℥i.
Syrupi.....	℥x.—Misce.

Mucilage of acacia is incompatible with both of the first two ingredients, forming a gelatinous semi-solid with chloride of iron, and being precipitated in a ropy rubber-like condition by alcohol in both. This, then, being the ingredient to be protected, if we first fortify the mucilage with the syrup, then add the other ingredients a few drops at a time, shaking thoroughly after each addition and giving time for the mucilage to overcome the attack before more is added, the result will be a bright, clear, ruby-red liquid.

When the reaction cannot be prevented by skill in mixing, or be materially retarded by the intervention of a viscid liquid, the mixture should be compounded with the intention of obtaining the precipitate in as fine a condition as possible, so that it will diffuse evenly through the mixture on shaking.

The incompatible bodies should be mixed in dilute solutions, and well shaken together.

Oftentimes the pharmacist is justified in either leaving out an incompatible ingredient, *when it has no decided medicinal value in the mixture*, but has been ordered simply as a solvent or adjuvant, or in adding a simple solvent, as alcohol or glycerin, to a mixture in order to hold in solution a body which would be precipitated in an aqueous liquid.

The two following mixtures will illustrate this:

R. Quinina sulphatis.....	℥ii.
Acidi sulphurici diluti.....	℥i.
Fldest. glycyrrhizæ.....	℥ss.
Syrupi.....	℥i.
Aquæ destillatæ.....	q. s. ut ft., ℥iv.—M.

Here the diluted sulphuric acid is ordered to dissolve the quinine sulphate, and the fluidextract of licorice to cover its intense bitterness (being one of the best agents for this purpose), but the prescriber has overlooked the fact that acids will precipitate the glycyrrhizin in the fluidextract of licorice, the real flavoring principle of the root, and thus the very object which he is seeking, a clear and palatable mixture, will be defeated.

To omit the acid is the only remedy for this. The quinine sulphate may be diffused through the mixture, and the licorice will then mask its bitterness. Dispense with a shake-label.

R.	Hydrargyri chloridi corros.	gr.i.
	Potassii iodidi	℥ii.
	Strychninæ sulphatis	gr.i.
	Tinc. cinchonæ compositæ	℥ii.
	Aquæ	ad ℥vi.—M.

The first two ingredients of this mixture form the well known Mayer's precipitant—double iodide of mercury and potassium—which will precipitate the strychnine and the active principles of cinchona from aqueous solutions, but the precipitates are all soluble in alcohol; consequently this incompatibility may be overcome by using enough alcohol to hold these in solution.

In the above case we may dissolve the corrosive sublimate and potassium iodide in two drachms of warm water, and the strychnine sulphate in two drachms more of water, mix the strychnine solution with the compound tincture of cinchona and add half an ounce of alcohol, then add the iodide solution and shake well. This makes a three-ounce mixture instead of a six-ounce, and the dose should be marked *one half of that ordered*, but the mixture now contains enough alcohol to hold the strychnine and cinchona alkaloids in solution, and the patient will take scarcely any more alcohol than in the mixture as ordered.

Strychnine should never be dispensed in solutions with iodides or bromides unless alcohol or some suspending agent be present.

INFUSIONS AND DECOCTIONS

These are much less frequently prescribed in America than in England and Europe, where their preparation is a daily task in the large stores.

Where they are frequently demanded conveniences for their preparation are kept at hand, but where only an occasional call is made for them they are more likely to be considered an annoyance.

They should not be considered merely as weak galenical preparations, though they are not as potent as other preparations. They differ materially from tinctures, fluidextracts, wines, etc., not only in strength, but also in taste and appearance, and oftentimes in action. This is because quite different principles are extracted from drugs by water than those which are obtained by alcoholic liquids. *In infusions and decoctions only the water-soluble principles are desired, and a diluted tincture or fluidextract is never a proper substitute.*

We all know the difference between a properly made cup of tea or coffee, and one made by diluting a fluidextract of tea or coffee with hot water. The latter lacks the refreshing qualities as well as the aroma and flavor of the former. So with drugs.

In digitalis, for instance, the infusion contains principles which are lacking in the tincture or fluidextract, and the superior results obtained by use of the infusion has long made it a favorite preparation of this drug.

Drugs containing volatile principles or principles easily injured by heat are best adapted for infusions, while drugs containing albuminous bodies, or principles not readily extracted, are made into decoctions. Cold infusions are prepared by percolation from drugs containing extremely volatile or sensitive principles (as infusion of wild cherry in which hydrocyanic acid is developed by cold water) or from drugs containing undesired principles which are not readily extracted by cold water (as infusion of cinchona).

The Pharmacopœial directions for preparing infusions are as follows:

"Put the substance" (50 Gm. coarsely comminuted) "into a suitable vessel provided with a cover, pour upon it the boiling water, cover tightly, and let it stand for half an hour. Then strain with pressure, and pass enough water through the strainer to make the infusion measure 1000 cc."

The strength of infusions is thus 5 per cent (50 Gm. of drugs for 1000 cc. of infusion), unless otherwise specified by the Pharmacopœia or the physician.

Earthenware vessels are best adapted for making infusions, because they are thick walled and hold the heat better than glass or metal. They are also not easily broken.



FIG. 2.—Infusion mug.



FIG. 1.—Infusion mug.

Infusion mugs are made, consisting of a cup-shaped vessel having a perforated basket or dipahragm of earthenware supported near the top, in which the drug is placed, and the boiling water is poured through this.

The full capacity of the mug should be made each time, the object of having the drug at the top of the mug being to allow of circulatory displacement as the maceration proceeds, thus insuring better extraction. The same result may be secured by tying the drug very loosely in a bag of thin cloth, which is then immersed just beneath the surface of the hot water. In the latter case an ointment pot, coffee cup, earthenware pitcher, coffee pot or any other suitable vessel which can be covered, may

be used, and only the desired amount of infusion made each time. A tall vessel of suitable capacity should be selected. Straining is also unnecessary, the process being practically automatic. The bag should be of thin cloth, not too tightly woven, and the drug should be enclosed loosely, not pressed into a ball. The vessel, whether an infusion mug or what, should first be heated by pouring into it some boiling water,

which is allowed to stand a few moments, then thrown out just before the infusion-water is poured in.

Hard water will not make a good infusion, and only rain or distilled water should be used; the quality of the infusion will depend almost as much upon the use of a good soft water, as upon the quality of the drug.

No advantage is gained by macerating overtime, but deterioration may result from it, as in making tea or coffee, when an astringent or bitter taste is developed by prolonged heating. Complete extraction is not always desired, but only the extraction of certain principles.

Infusions should never be filtered. They spoil quickly, and should therefore be made fresh, and in small quantities. In a few cases (Infusion of Digitalis, Gentian Compound, etc.), a small proportion of alcohol is added to the infusion for the purpose of preserving it; but this should never be done without the sanction of the authority.

Concentrated infusions, made four or six times the strength of the official, are objected to in some cases for this reason. They are nearly always made to contain alcohol as a preservative, and this may be objectionable even in the small quantity which exists after diluting the infusion. Probably the best method of preserving infusions, concentrated or otherwise, is to proceed according to the rules of sterilization. First sterilize the bottle by the use of boiling water, which is allowed to stand in the bottle for some time; then pour in the infusion *while hot*, filling the bottle to the neck, and cork immediately. In this way infusions, made by the hot process, may be preserved for weeks, without material change. Concentrated infusions, if preserved in this manner, should be stored in small bottles, and the entire contents of a bottle diluted and used when opened.

They may be stored in large bottles, and the contents withdrawn as desired, by the method proposed by Prof. Almen, of Sweden.

The bottle is fitted with a stopper having two perforations. Through one of these perforations a vent-tube passes, reaching to just inside the bottle; the outer end of the tube is plugged loosely with absorbent cotton. The short end of a glass-syphon is passed through the other perforation, the long end being provided with a tap, made of a closely-fitting piece of rubber tubing and a pinchcock.

The contents of the bottle are thus withdrawn through the syphon, and the air which enters the bottle is sterilized by filtering through the cotton. The apparatus requires to be sterilized each time before refilling, by means of boiling water.

Decoctions are directed to be made as follows: "Put the substance" (50 Gm. coarsely comminuted) "into a suitable vessel provided with a cover, pour upon it 1000 cc. of cold water, cover it well, and boil for fifteen minutes. Then let it cool to about 40° C. (104° F.), express, strain the expressed liquid, and pass enough cold water through the strainer to make the product measure 1000 cc."

The general strength of decoctions is thus the same as infusions, but the method of preparation differs. Decoctions are made by putting the drug into *cold* water, which is then brought to a boil, and the boiling continued for fifteen minutes, then allowed to cool and strained. Better extraction is thus obtained than if the drug were placed directly in boiling water. In the latter case albuminous

bodies in the drug would be suddenly coagulated, and entangle some of the principles which it is desired to extract. This is avoided by the gradual heating. These albuminous bodies are not likely to be found in drugs adapted for infusion:

The apparatus used may be the same as that for infusion, with the double advantage of preventing the burning of the drug by having it suspended in the top of the liquid. This is quite likely to occur where the drug is allowed to settle at the bottom of the vessel. Metallic vessels are more desirable for decoctions than for infusions, owing to the necessity of heating by direct flame; but iron should not be used, because it produces a black coloration with tannins. With care, earthenware vessels are almost as convenient, and more cleanly.

Previous maceration of the drug in cold water is advantageous, but a prolonged boiling is injurious, because the principles are altered thereby. Violent ebullition is also to be avoided; a gentle simmering being all that is necessary.

A tall vessel is also better than a shallow one; and boiling is hastened by covering the vessel.

Since boiling water extracts vegetable principles more easily than cold water, some of these may be thrown out of solution on cooling: straining is therefore performed at a definite (tepid) temperature, and any principles afterward deposited are diffused by shaking.

Decoctions are seldom clear and should not be filtered.

The precautions in the use of water, and preservation, alluded to under infusions, apply also to decoctions.

LOTIONS, LINIMENTS, ETC.

These present no special difficulties, being practically mixtures for specific purposes.

Lotions frequently contain insoluble bodies which should be in a condition to diffuse easily when the liquid is shaken. Gums are sometimes added to emulsify camphors and resinous bodies, but should be used sparingly. The application of a thin mucilage to the skin is not agreeable where it is allowed to dry. Better results are obtained as a rule by means of very fine powders or precipitates.

Liniments may be oily, saponaceous or alcoholic liquids. The first partake of the nature of soft ointments and are applied by rubbing. The second are both stimulating and soothing. They are sometimes made extemporaneously by the admixture of an oil and an alkali, as in soap and lime liniments. The oil and alkali should be mixed at once instead of gradually, and vigorously shaken.

Alcohol favors the union of the oil and alkali and is frequently added for this purpose. Oleic acid also promotes saponification, and the addition of a few drops sometimes aids in the preparation of such.

When an alcoholic liquid is ordered with an alkali and an oil, the alcoholic body, or a portion of it, may be added to the alkali before shaking with the oil.

Alcoholic liniments are stimulating or anodyne, and are used mostly for painful affections, as sprains, bruises, neuralgias, etc. They present no difficulties unless an insoluble salt is ordered, or an

aqueous fluid is directed to be incorporated. Sometimes a corresponding alcoholic liquid can be substituted for the aqueous, in the latter case, as in solutions of iodine and ammonia.

Liniments should be plainly marked "For External Use" and dispensed in a poison bottle. Lotions which are to be used as injections are dispensed in the ordinary vials and marked plainly, but not marked poison unless so ordered on the prescription.

A red label is used for these by preference.

COLLYRIA

Solutions intended for use in the eye are generally simple in character, but require the most scrupulous care in their preparation.

A few specks of dust in the bottle, or a small bit of undissolved salt or other matter may cause intense pain and lead to serious results. Only distilled water should be used in the preparation of these solutions, and it is well also to rinse the bottle which is to contain the solution with distilled water before filtering the liquid into it. If more salt is ordered in a collyrium than can be dissolved in the quantity of solvent prescribed, a cold saturation should be made and the undissolved salt filtered out.

Likewise in making alum-curds, by shaking alum with milk or with the whites of eggs until coagulation ensues, powdered alum should not be used because it cannot be removed completely from the coagulum, and if retained the sharp edges will irritate the inflamed surface.

MIXTURES

A. Simple Solutions

- I

R. Zinc sulphat..... gr. iv Sat. sol. boric acid..... ʒ iv M. Ft. collyrium. Sig.—Eye drops	Triturate the zinc sulphate and 73 grs. of boric acid with the water, gradually added, until the salts are dissolved, then filter. Or, heat 4 fluidounces of water to boiling, add the boric acid, stir until dissolved, cool, replace the water that evaporated, add the zinc sulphate and when this is dissolved, filter.
---	--
- 2

R. Ferri citratis..... ʒ ij Aquæ..... ʒ ij M. Ft. solut. Sig.—Citrate of iron.	Warm the water, but do not heat to boiling, drop the citrate into it and agitate until dissolved. Do not powder the citrate in a mortar.
--	---
- 3

R. Acaciæ..... 35.0 Gm. Sodium benzoate..... 0.1 Gm. Aquæ..... ad. 1000. cc. M. Ft. solut. Sig.—Mucilage of acacia.	Weigh a 4 oz. wide-mouthed bottle, with a cork and a 3 inch square of thin cloth. Place the acacia in the cloth and run a stream of water with moderate force over or through it for a moment. Then tie the acacia and sodium benzoate in a bag of the wet cloth, and suspend in the bottle in which has been placed the water, so that the bag hangs just beneath the surface of the water. When the gum has all dissolved, remove the empty bag.
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4

- R. Chloroform.....
 Distilled water, each a sufficient quantity.
 Sig.—Chloroform water, U. S. P.

"Add enough chloroform to a convenient quantity of distilled water, contained in a dark amber-colored bottle, to maintain a slight excess of the former, after the contents have been repeatedly and thoroughly agitated. When chloroform water is required for use, pour off the needed quantity of the solution, refill the bottle with distilled water and saturate it by thorough agitation, taking care that there be always an excess of chloroform present."

Make 4 ounces, using 0.5 cc. of chloroform.

5

- R. Oil of bitter almond..... 1 cc.
 Distilled water..... 1000 cc.
 Sig.—Bitter almond water.

Dissolve the oil in the water by agitation.

6

- R. Olei cinnamomi..... 0.20
 Talcum..... 1.50
 Aquæ destillatæ..... 100.0
 M. Ft. solut. s. a.
 Sig.—Cinnamon water.

Rub the oil with the talcum in a mortar, gradually add the water, then filter, returning the first portions to the funnel until the filtrate comes through clear. Finally add enough water through the filter to make 100 cc. of filtrate.

7

- R. Olei menthæ piperitæ..... 0.20
 Magnesii carbonatis..... 0.50
 Aquæ destillatæ..... 100.0
 M. Ft. solut. s. a.
 Sig.—Peppermint water.

Rub the oil with the magnesium carbonate, gradually add the water, filter and pass enough water through the filter to obtain 100 cc.

8

- R. Olei anisi..... 0.20
 Calcii phosphatis precip... 0.60
 Aquæ destillatæ..... 100.0
 M. Ft. solut. s. a.
 Sig.—Anise water.

Rub the oil with the calcium phosphate, and proceed as above.

9

- R. Olei gaultheriæ..... 0.20
 Gossypii purificati..... 0.40
 Aquæ q. s..... ad. 100.00
 M. Ft. solut. s. a.
 Sig.—Wintergreen water.

Drop the oil upon the cotton, distribute it well by picking. Place a small pellet of fresh cotton in the apex of a funnel, pack the oiled cotton over it, press down firmly, and pour water through the whole until 100 cc. of percolate is obtained.

10

- R. Olei fœniculi..... 0.20
 Aquæ destillatæ..... 100.00
 M. Ft. solut. s. a.
 Sig.—Fennel water.

Drop the oil upon filtering paper, distributing it over as large a surface as possible, let the paper absorb it, then drop the paper into 100 cc. of warm water, shake well two or three minutes, then filter.

11

- R. Lime..... 6.25 Gm.
 Distilled water, a sufficient quantity.
 M. Sig.—Lime water.

"Slake the lime by the gradual addition of 12.5 cc. of distilled water, then add 335 cc. more of distilled water, and agitate occasionally during half an hour. Allow the mixture to settle, decant the liquid and throw it away. Then add to the residue sufficient water to make about 1000 cc., agitate thoroughly, wait a short time for the coarser particles to subside, and pour the liquid, holding the undissolved lime in suspension, into a glass-stoppered bottle. From time to time shake the bottle, so as to keep the solution saturated."

Pour off the clear liquid when it is wanted for use.

12

- R. Tincture of ferric chlorid 40 cc.
 Diluted acetic acid..... 60 cc.
 Solution of ammonium acetate..... 500 cc.
 Aromatic elixir..... 120 cc.
 Glycerin..... 120 cc.
 Water, a sufficient quantity to make..... 1000 cc.
 M. Sig.—Basham's mixture.

"To the solution of ammonium acetate (which should not be alkaline) add successively, the diluted acetic acid, the tincture of ferric chlorid, the aromatic elixir, and the glycerin, and, lastly, enough water to make the product measure 1000 cc. This preparation should be freshly made.

Make four fluidounces.

13

- R. Solution of lead subacetate..... 35 cc.
 Distilled water, a sufficient quantity to make 1000 cc.
 M. Sig.—Lead water.

"Mix the solution of lead subacetate with enough distilled water, previously boiled and cooled, to make the product measure 1000 cc. Keep the solution in well-stoppered bottles."

Make four fluidounces. The solution should be clear. Only distilled water free from gases can be used in this preparation.

14

- R. Tannic acid..... 20 Gm.
 Sodium citrate..... 1 Gm.
 Oil of rosemary..... 10 cc.
 Glycerin..... 79 Gm.
 M. Sig.—Glycerite of tannic acid.

Weigh the tannic acid, sodium citrate and glycerin successively, into a tared bottle and apply the heat of a water-bath until all is completely dissolved.

Make one-fifth the quantity.

15

- R. Soap, dried..... 60 Gm.
 Camphor, in small pieces 45 Gm.
 Oil of rosemary..... 10 cc.
 Alcohol..... 700 cc.
 Water, a sufficient quantity to make..... 1000 cc.
 M. Sig.—Soap liniment.

Dissolve the camphor and oil of rosemary in the alcohol, then add the soap and enough water to make 1000 cc. and shake until the soap is dissolved. Set it aside, in a cool place, for twenty-four hours, and filter.

Make 100 cc.

16

R.	Ammonium carbonate, in translucent pieces	34 Gm.
	Ammonia water.....	90 cc.
	Oil of lemon.....	10 cc.
	Oil of lavender flowers..	1 cc.
	Oil of nutmeg.....	1 cc.
	Alcohol.....	700 cc.
	Distilled water, a suffi- cient quantity to make	1000 cc.
M.	Sig.—Aromatic spirit of am- monia.	

To the ammonia water, contained in a flask, add 140 cc. of distilled water, and dissolve the ammonium carbonate in the liquid. Allow to stand twelve hours. Introduce the alcohol into a graduated cylinder, add the oils, then gradually add the solution of ammonium carbonate, and afterward enough distilled water to make the product measure 1000 cc. Set the liquid aside during twenty-four hours in a cool place, occasionally agitating. Keep the product in glass-stoppered bottles, in a cool place.

Make 100 cc. The liquid should be nearly clear without filtration. If any considerable amount of salt remains undissolved after twenty-four hours, shake frequently until it dissolves.

17

R.	Tinct. ferri chlorid.....	℥ ij
	Spt. aethylis nitrit.....	℥ iv
	Mucilag. acaciæ.....	℥ i
	Syrupi q. s. ut ft.....	℥ iij
M.	Sig.—Coch. parv. t. i. d. post cibo.	

Mix the iron with two drachms of syrup and the spirit with three drachms of syrup. Mix the mucilage with the remainder of the syrup and gradually add, first the diluted spirit of niter, then the diluted tincture. May also be mixed by adding the spirit and tincture very slowly to the mucilage previously mixed with the syrup.

18

R.	Sodii bicarbonatis.....	℥ iv
	Tinct. zingiberis.....	℥ j
	Tinct. gent. comp.....	℥ vj
	Aquæ menth. virid.....	℥ iij
M.	Sig.—Capiat cochleare parvum post prandium.	

19

R.	Potassii bromidi.....	gr. xv
	Spiritus ammon. aromat.....	℥ j
	Syrupi.....	℥ iij
	Aquæ.....	q. s. ad. ℥ ij
M.	Ft. haustis. Sig.—Detur statim.	

20

R.	Iodi.....	℥ j
	Spiritus camphoræ.....	℥ iv
	Acidi carbolici.....	℥ ss
	Aquæ ammoniæ.....	℥ iv
M.	Sig.—For inhalation.	

Dissolve the iodine and carbolic acid in the spirit of camphor and slowly add the aqua ammonia to this. (A clear colorless solution results.)

21

R.	Potassii chlorat.....	℥ j
	Acid salicylici.....	℥ j
	Tinct. ferri chlor.....	℥ j
	Glycerini.....	℥ j
	Aquæ.....	℥ iv
M.	Ft. gargar. Sig.—"Salicylated gargle."	

Dissolve the salicylic acid in the glycerin by aid of a gentle heat, and the chlorate in the water. Mix the two solutions and add the tincture of iron.

22

R.	Ammonii chlorid.....	0.250
	Zinci sulphatis.....	0.500
	Camphoræ.....	0.150
	Aquæ destillat.....	40.0
	Alcoholis.....	6.0

M. Ft. collyr. Sig.—Eye drops.

Dissolve the camphor in the alcohol, and the salts in the water; mix the two solutions and shake until the liquid has become clear, then filter.

(This preparation, with the addition of 0.040 Gm. of Spanish saffron, macerated in the liquid for twenty-four hours, then filtered, is often prescribed under the name of "Collyrium Astringens Luteum.")

23

R.	Potassii chloratis.....	3 ii
	Acidi borici.....	5 ii
	Acidi tannici.....	3 i
	Aquæ.....	3 xii

Sig.—Apply locally.

Makes a clear mixture which soon deposits—mostly tannin. The use of 1½ oz. of glycerin produces a permanently clear solution.

24

R.	Liq. hydrogenii dioxidi	
	Glycerini..... aa	3 ii

If the glycerin is free from iron this mixture is quite stable.

25

R.	Ætheris.....	3 iss
	Chloroformi.....	3 j
	Tinct. iodi.....	3 ss
	Tinct. camphoræ.....	3 ss
	Olei picis liquid.....	3 ij

M. Sig.—Inhale as vapor.

26

R.	Acid salicylici.....	1.0
	Acid lactici.....	1.0
	Acid acetici glac.....	1.0
	Collodii.....	20.0

M. Ft. solut.

Sig.—Corn and wart collodion.

27

R.	Hydrarg. chlorid corros....	gr. xvj
	Collodii.....	3 ss

M. Ft. solut.

Sig.—Apply as directed.

Corrosive sublimate dissolves very slowly in collodion. By dissolving it in half a drachm of warm alcohol and mixing with the collodion, the prescription can be dispensed quickly.

28

R.	Sodii phosphatis.....	3 iv
	Glycerini.....	3 iv

Misce.

The substitution of Solution of Sodium Phosphate, N. F. for the crystalline salt would make a presentable mixture.

29

R.	Cydonii contusi.....	gr. xv
	Aquæ bullientis.....	3 ivss
	Ft. mucilago et adde.	
	Glycerini.....	3 vj
	Spiritus odorati.....	3 ss

M. Sig.—Toilet lotion.

Make the mucilage by macerating quince-seed in the hot water for three to four hours, then strain.

30

R.	Camphor, in coarse powder.....	200 Gm.
	Cotton-seed oil.....	800 Gm.

M. Sig.—Camphor liniment.

Introduce the camphor and cotton-seed oil into a suitable flask, and heat gently until the camphor is dissolved. Make 50 Gms.

31

R.	Cocainæ muriatis.....	gr. v
	Mentholi.....	gr. v
	Acidi carbolicæ.....	gr. ij
	Alboleni liquidii.....	3 ij

M. Ft. nebula.

Cocaine alkaloid must be used in place of the hydrochloride. A clear solution will then be obtained.

32

R.	Resorcini.....	gr. x
	Mentholi.....	gr. v
	Camphoræ.....	gr. v
	Petrolati liquidi.....	$\frac{3}{4}$ iv
M.	Ft. nebula.	

Dissolve the resorcin in an ounce of almond oil (expressed) and the other ingredients in three ounces of liquid petrolatum. Mix the solutions, and filter if necessary.

33

R.	Mentholi,	
	Thymoli.....aa	gr. x
	Olei eucalypti.....	$\frac{3}{4}$ ss
	Phenoli.....	gr. vj
	Acidi borici.....	gr. x
	Petrolati liquidi.....	$\frac{3}{4}$ j
M.	Ft. nebula.	

The boric acid will not dissolve, and should be omitted.

34

R.	Iodi	
	Mentholis	
	Camphoræ.....aa	gr. ss
	Petrolati liquidi.....	$\frac{3}{4}$ i
M.	Ft. nebul.	

Dissolve (completely) the iodine in the liquid petrolatum, add the menthol, dissolve and lastly dissolve the camphor. Successive solutions are necessary to secure a clear product.

35

R.	Camphoræ.....	gr. ss
	Mentholis.....	gr. ss
	Glycerini.....	$\frac{3}{4}$ ii
	Sodii bicarb.....	gr. iii
	Petrolati liquidi.....ad	$\frac{3}{4}$ iv
M.	Sig.—Ear drops.	

Dissolve the camphor and menthol in the liquid petrolatum and add a little lanolin. Dissolve the bicarbonate in the glycerin and add to the oil solution. An emulsion-like mixture is obtained which remains in suspension. (Lascoff.)

36

R.	Resorcinol.....	0.3
	Mentholis.....	0.2
	Petrolati liq.....	30.0
M.	Ft. nebula.	

Dissolve the menthol in the liq. petrolatum. Dissolve the resorcin in about 5 minims of alcohol and add. A clear mixture results. (Lascoff.)

37

R.	Cocainæ chlorid.....	0.2
	Sol. adrenalin chlor.....	6.0
	Mentholis.....	0.1
	Petrolati liquidi.....ad	30.0
M.	Ft. nebul.	

Use adrenalin inhalant in place of solution of adrenalin chloride. Dissolve cocaine alkaloid in the liquid petrolatum and add the menthol and inhalant. (Lascoff.)

38

R.	Hydrargyri salicylatis in	
	albolini 20 per cent.....	$\frac{3}{4}$ i
M.	Sig.—Use for injection.	

Mix the mercury salicylate with 5 grs. of lanolin and triturate with the albolene gradually added. A smooth emulsion results. (Lascoff.)

B. Compound Solutions

39

R.	Arsenic trioxide.....	10 Gm.
	Diluted hydrochloric acid	50 cc.
	Distilled water, a sufficient	
	quantity to make...	1000 cc.
M.	Sig.—Valangin's solution.	

"Mix the diluted hydrochloric acid with 250 cc. of distilled water, add the arsenous acid, and boil the mixture until all the arsenic is dissolved. Filter the solution and pass enough distilled water through the filter to make the product measure 1000 cc. Mix thoroughly."

Make 100 cc.

40

- R. Arsenic trioxide, in fine powder..... 10 Gm.
 Potassium bicarbonate... 20 Gm.
 Compound tincture of lavender..... 30 cc.
 Distilled water, a sufficient quantity to make... 1000 cc.
- M. Sig.—Fowler's solution.

"Boil the arsenic trioxide and potassium bicarbonate with 100 cc. of distilled water, until solution has been effected. Then add enough distilled water to make the solution, when cold, measure 970 cc. and add the compound tincture of lavender. Filter through paper."

Make 100 cc.

41

- R. Hydrargyri biniodidi..... gr. ij
 Syr. sarsaparillæ comp..... 3 ij
- M. Sig.—One teaspoonful 3 times a day.

The red iodide must be dissolved by aid of a few grains of potassium iodid (about 10 grains) and water (one drachm). It would be dangerous to dispense exactly as written.

42

- R. Lime..... 65 Gm.
 Sugar..... 350 Gm.
 Water, a sufficient quantity to make..... 1000 cc.
- M. Sig.—Syrup of lime.

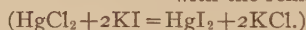
Slake the lime by the addition of 35 cc. of water and mix with the sugar in a mortar, so as to form a homogeneous powder, then add to the mixture 500 cc. of boiling water, contained in a bright copper or tinned iron vessel, boil for five minutes, constantly stirring. Dilute the liquid to 950 cc. with water and filter through white paper. Then add to it enough water to make the product measure 1000 cc. and mix thoroughly. Keep the syrup in well-stoppered bottles.

Make 100 cc. The syrup should be white, or nearly so.

43

- R. Hydrarg. biniodidi..... 0.400
 Potassii iodidi..... 6.000
 Aquæ..... 180.000
- M. Ft. Solut. Sig.—2 C.c. per dose.

To make the red iodid of mercury dissolve 0.240 Gm. of corrosive sublimate in 20 cc. of hot water, and 6.3 Gm. of potassium iodid in 20 cc. of water and mix the two solutions. Dilute with the remaining water.



0.24 Gm. of HgCl_2 and 0.30 Gm. of KI are required to make 0.40 Gm. of HgI_2 .

44

- R. Quininæ sulphatis..... 2.0
 Acidi sulphurici dilut..... q.s.
 Aquæ..... 60
- M. Ft. solut. Sig.—Coch. med. omnia hora.

Mix the quinine with half the water, add acid drop by drop until a clear solution is obtained, and then add the rest of the water. State how much acid was used.

45

- R. Tinct. ferri chlorid..... 3 j
 Quininæ sulph..... ʒ j
 Acid sulphuric dil..... q. s.
 Aquæ..... q. s. ad. 3 ij
- M.

No acid is needed, the quinine being soluble in the tincture of iron.

46

- R. Theobrominæ..... ʒ ss
 Sodii salicylatis..... ʒ ii
 Aquæ menthæ piper..... ʒ iii

Requires about 10 minims of solution of sodium hydroxide to make a clear solution.

47

R.	Iodi.....	gr. iss
	Potassii iodidi.....	gr. iij
	Syrupi aurantii.....	℥ j
	Aquæ.....	℥ iij
M.	Ft. solut.	

Dissolve the potassium iodid in two drachms of water and the iodine in this solution. Add the syrup, then the remainder of the water.

48

R.	Sodii boratis.....	3.0
	Mellis.....	30.0
	Misce fiat linctus.	
Sig.	—For sore mouth.	

Honey acts upon borax in the same way as does glycerin, but less energetically.

Free boric acid (?) and sodium metaborate are formed in the above by action of the honey upon the borax.

49

R.	Acid gallic.....	℥ j
	Potass. citrat.....	℥ iss
	Aquæ.....	℥ iv
M.	Ft. solut.	

The gallic acid is entirely dissolved by the potassium citrate solution.

50

R.	Acidi salicylici.....	℥ ij
	Sodii boratis.....	℥ iij
	Glycerini.....	℥ iiss
	Aquæ.....	ad. ℥ viij
M.	Sig.—Gargle.	

Dissolve the borax in the glycerin by aid of heat, add the salicylic acid and continue a gentle heat until dissolved, then add the water.

If the borax be dissolved in the water and the salicylic acid added, the latter will be dissolved, but will be thrown out of solution when the glycerin is added by reason of the decomposition of the borax. On warming a permanent solution is formed.

51

R.	Tinct. tolu.....	℥ ij
	Syrupi senegæ.....	℥ iv
	Acidi acetici.....	℥ iss
	Syr. pruni virgin.....	ad. ℥ iv
M.	Sig.—A teaspoonful as required.	

Add the tincture to the acid, then mix with the syrups. Acetic acid resembles alcohol in solvent powers.

52

R.	Olei picis liquidi.....	℥ ij
	Magnesii carbonatis.....	℥ ij
	Aquæ.....	O i
	Misce, filtra et adde	
	Iodi.....	gr. x
	Potassii iodidi.....	℥ ss
M.	Ft. solut.	
Sig.	—Use with inhaler.	

Triturate the oil of tar with magnesium carbonate, add the water gradually and filter. Dissolve the potassium iodide in about half an ounce of this filtrate and the iodine in this solution, and mix with the rest.

53

R.	Sodii salicylatis.....	℥ ij
	Tinct. ferri chlorid.....	℥ ij
	Acidi citrici.....	gr. v
	Glycerini.....	℥ vj
	Ol. gaultheriæ.....	m. iv
	Liq. ammonii citratis..	ad. ℥ ij
M.	Ft. solut. s. a.	
Sig.	—Salicylated iron mixture.	

Dissolve the sodium salicylate and citric acid in the solution of ammonium citrate. Add the tincture of iron to the glycerin, then mix the two solutions; finally add the oil of wintergreen and shake well. (Salicylates are incompatible with tincture of iron, but precipitation is prevented by the ammonium citrate.)

54

- R. Hydrarg. chlorid corros. . . . gr. ii
 Chloralis hydratis. ℥ iv
 Zinci sulphatis. ℥ ii
 Quininæ chloridi. ℥ i
 Alcoholis. ℥ i
 Aquæ. ℥ iii
- M. Sig.—For external use.

The quinine chloride and zinc sulphate react to form quinine sulphate, a portion of which remains undissolved. Use an equivalent (75 grs.) of quinine bisulphate, and a clear mixture results. (Dunning.)

55

- R. Hydrarg. iodid rub. gr. xx
 Potass. iodid. gr. xl
 Atropinæ sulph. gr. iss
 Tinct. lavandul. co. ℥ i
 Glycerini. ℥ vii
- M. Ft. sol. Sig.—For external use.

Dissolve the iodides in ℥iv glycerin by aid of heat. Dissolve the atropin in the tincture and rest of the glycerin, and when the first solution is cool, mix. Remains clear for some time.

56

- R. Ferri et quin. cit. ℥ i
 Tinct. ferri chlor. ℥ i
- M. Ft. sol.

Use 168 minims of solution of ferric chloride and water to make an ounce in place of the tincture.

57

- R. Hydrargyri biniodidi. 0.5
 Olei ricini. 25.0
 Olei sesami. 25.0
- M. Ft. solut.

Rub the mercuric iodid with a little of the castor oil, then add the rest of the oils, heat until solution is effected, and filter. (Dunning.)

58

- R. Tinct. ferri chlor. ℥ iv
 Syr. hypophosph co. ℥ vss
- M. Sig.—Teaspoonful after each meal.

Makes a muddy, viscid mass. Tincture of citrochloride of iron would make a clear mixture.

59

- R. Tinct. ferri citrochlor. ℥ ii
 Acid phosphorici dil. ℥ iii
 Glycerini. ℥ iv
 Elixir aromat ad. ℥ iv

Phosphoric acid precipitates the iron. Precipitate is soluble in excess of sodium citrate or phosphoric acid. No precipitate formed if tincture of ferric chloride is used.

60

- R. Sodii salicylatis. ℥ iii
 Sodii bicarbonatis. ℥ ii
 Tinct. ferri chlorid. ℥ ii
 Aquæ menth pip ad. ℥ vi

Dissolve the salicylate and bicarbonate in five ounces of peppermint water and slowly add the tincture of iron with constant stirring. When effervescence has ceased add peppermint water to make 6 fluidounces. Makes a clear, deep-red solution.

61

- R. Sodii salicylatis. ℥ i
 Potass. bicarb. ℥ iss
 Tr. ferri chlorid. ℥ i
 Tr. nucis vomic. M xl
 Spir. chloroformi. ℥ iss
 Aquæ menth pip. ad. ℥ iv
- Sig.—Dose one tablespoonful.

Makes a clear, purplish liquid.

62

- R. Tinct. nucis vomicæ
 Liq. potass. arsenit. aa 3 iii
 Ferri pyrophosph. 3 iss
 Sodii bromidi. 3 vi
 Elixir lactopeptin. ad 3 iv
 M. Ft. sol.

The acid in the elixir throws out some of the iron. The pyrophosphate must be dissolved separately in about 3 drachms of warm water, and ammonia water used cautiously to secure a clear solution, after mixing.

63

- R. Quininæ sulphatis 3 iii
 Acidi nitrici. 3 ii
 Ferri sulphatis. 3 iii
 Potass. nitratis. 3 ii
 Aquæ. q. s. ad. 3 iv

Dissolve the quinine sulphate in the nitric acid by aid of a little heat and add a grain of sugar to produce brown fumes in the mixture. Dissolve the iron sulphate and potass. nitrate in about 3 ounces of warm water and pour into the quinine mixture. A bright red liquid results. If the nitric acid is free from nitrous acid—and no sugar is used—the color will be pale green, very slowly turning red on standing.

64

- R. Lithii citratis. 3 ii
 Vini colchici. 3 i
 Liq. ferri et ammon acet. 3 iii

The citrate changes the red color of the iron solution to green.

65

- R. Acidi acetylsalicylici. gr. xv
 Potassi acetatis. gr. xl
 Syrupi. 3 i
 Aquæ. ad. 3 ii
 M. Ft. sol.

The potassium acetate will almost dissolve the acetylsalicylic acid (60 grains entirely so) but the acid will soon hydrolyse and split up in solution.

66

- R. Acidi acetylsalicylici. 3 i
 Elix. sodii salicylat. comp. 3 ii
 M. Sig.—3i t. i. d.

The acid is not entirely soluble in the elixir, but it is gradually decomposed, and crystals of salicylic acid separate which are irritating. Acetylsalicylic acid is not suitable for administration in solution, but it is better to dissolve it by aid of (about 1 drachm of) sodium citrate than to administer salicylic acid in crystals.

67

- R. Codeinæ sulph. gr. iv
 Ammon. chlorid. 3 iss
 Aspirin. 3 iss
 Aquæ. 3 ii
 Syrupi aurantii. ad. 3 iv

The aspirin may be dissolved by aid of sodium citrate (about 3iii) or by sodium bicarbonate (about 84 grains) or dispensed as a shake mixture. In any case it will decompose fairly rapidly.

C. Gaseous Solutions

68

- R. Ammonii carbonat. 5.0
 Acidi acetic diluti. 100.0
 M. Ft. solutio.
 Sig.—“Spirit of Mindererus.”

Select clear pieces of ammonium carbonate, weigh carefully, and add gradually to the acid contained in a capacious vessel.

69

- R. Potassium bicarbonate.. 8 Gm.
 Citric acid..... 6 Gm.
 Distilled water, a sufficient quantity to make 100 cc.
 M. Sig.—Solution of potassium citrate.

Dissolve the potassium bicarbonate and the citric acid, each in 40 cc. of distilled water. Filter the solutions separately, and wash the filters with enough water to obtain, in each case, 50 cc. Mix the two solutions, and, when effervescence has nearly ceased, transfer the liquid to a bottle. This preparation should be freshly made.

70

- R. Magnesium carbonate.. 15 Gm.
 Citric acid..... 35 Gm.
 Syrup..... 60 cc.
 Oil of lemon..... 0.1 cc.
 Purified talc..... 5.0 Gm.
 Potassium bicarbonate.. 2.5 Gm.
 Water, a sufficient quantity to make about.. 350 cc.
 M. Sig.—Solution of citrate of magnesia.

Dissolve the citric acid in 250 cc. of hot distilled water. Gradually add the magnesium carbonate and stir until it is dissolved. Add the syrup, heat the liquid to the boiling point and immediately add the oil of lemon previously titrated with the talc and filter the mixture, while hot, into a strong bottle of suitable capacity. Add enough distilled water to make the product measure 350 cc. and when cold add the potassium bicarbonate and stopper the bottle securely. Lastly, shake the mixture occasionally, until the potassium bicarbonate dissolves.

71

- R. Acidi salicylici,
 Sodii bicarbonatis..... 5ā 3 ij
 Aquæ..... 3 iij
 M. Sig.—“Salicylate of soda solution.”

Place the acid in a pint mortar, rub to a paste with water and slowly add the sodium bicarbonate.

In the above reaction about two and a half pints of CO₂ are liberated and the effervescence is too violent to control in a three-ounce bottle. The solution gradually darkens owing to the excess of alkali present.

72

- R. Potassii chloratis..... 3 j
 Acidi hydrochlorici..... 3 j
 Aquæ destillatæ..... 3 iv
 M. Sig.—“Throat mixture.”

Compound in two ways.

(a)—Place the chlorate in bottle, add the acid, agitate for a moment, then add the water gradually.

(b)—Dissolve the chlorate in the water and add the acid to this solution.

73

- R. Potassii chloratis..... 3 ij
 Acidi hydrochlorici..... 3 ss
 Spiritus gualtheriæ..... 3 iiss
 Syrupi..... 3 iss
 Aquæ..... ad. 3 iv
 M. Sig.—“For ulcerated throat.”

The presence of syrup and flavoring in this shows that it is not intended for a solution of chlorin gas.

74

- R. Sodii boratis..... 1.80
 Sodii bicarbonatis..... 1.80
 Phenoli liq..... 0.36
 Glycerini..... 4.20
 Aquæ..... 120.0
 M. Ft. solut.
 Sig.—“Dobell's solution, N. F.”

Dissolve the salts in about half the water, add the glycerin and the carbolic acid and let stand one-half hour, then add enough water to make 120 cc.

75

- R. Acid salicylic..... 3 ij (Note the color.)
 Ammon. carbonat..... 3 vj
 Syrupi..... 3 iij
 Aquæ..... ad. 3 viij
 M. Sig.—Ammonium salicylate.

76

- R. Ammon. chlorid..... 3 j Use powdered ammonium chlorid,
 Ammon. carbonat..... 3 j and triturate the salts well with the
 Tinct. ipecac..... 3 j syrup of squill, add the tincture, warm
 Syrupi scillæ..... 3 viij to hasten the reaction, and when effe-
 Syrupi..... 3 j vescence has ceased add the syrup.
 M. Sig.—Pro tusse.

77

- R. Syr. scillæ..... 3 iv The nitrous ether is separated
 Syr. ipecacuan..... 3 ii from solution and slowly escapes as
 Spir. æth. nitrit..... 3 iij an effervescence. Cannot be avoided.
 Syr. pruni virg..... 3 ii (Dunning.)

78

- R. Potassii bicarbonatis..... 3 iij Syrup of tolu contains free acid
 Potassii citratis..... 3 i unless made by means of magnesium
 Tinct. hyoscyami..... 3 iij carbonate. In the latter instance there
 Syrupi tolu..... ad. 3 iij is no effervescence.
 M. Sig.—A teaspoonful every two
 hours.

D. Mixtures

79

- R. Potassii bromidi..... 3 ij Place in a bottle and shake until the
 Aquæ camphoræ..... 3 ij bromid is dissolved. Do not filter.
 M. Ft. solut.
 Sig.—"Bromide mixture." *Shake.*

80

- R. Hydrarg. chlorid corros 0.75 Gm. Dissolve the corrosive sublimate in
 Aquæ bullientis..... 9.00 cc. the boiling water, in a test-tube, add to
 Liquoris calcis... ad 250.00 cc. the lime water and shake.
 M. s. a. Sig.—"Yellow wash." *Shake.*

81

- R. Hydrarg. chlorid mitis. 8.75 Gm. Triturate the calomel lightly with the
 Aquæ..... 15.00 cc. water and add the lime water, con-
 Liquoris calcis... ad 1000 cc. stantly stirring. Make four ounces.
 M. "Black wash." *Shake.*

82

- R. Zinc chloridi..... 1.00 Make the zinc chlorid for this by care-
 Hydrarg. subchloridi..... 0.50 fully measuring 5.5 cc. of diluted
 Liquoris calcis..... 240.00 hydrochloric acid, to which add about
 M. Ft. lotio. Sig.—"Zinc and Mer- 1.0 Gm. of zinc oxide, then warm gently
 cury wash." Add this solution to the calomel and
 lime water previously mixed. If the
 zinc chloride be added to the lime water
 first, a *white* lotion results; if the calomel
 is added first, a *black* lotion will be
 obtained.

83

- R. Cupri sulphatis,
Zinci sulphatis..... aa 3 j
Liq. plumbi subacet..... 3 iss
Acid acetic dilut..... 3 xij
M. et filtrata. Sig.—"Villate's
solution."

Dissolve the zinc and copper salts in the diluted acetic acid, add the solution of subacetate of lead and agitate thoroughly. Filter through a small filter. To the filtrate add one drachm of starch, shake well and again filter.

84

- R. Zinci sulphatis..... 0.52
Plumbi acetatis..... 0.325
Tinct. catechu comp..... 4.0
Tinct. opii..... 2.0
Aquæ..... 100.0
M. Sig.—Inject as directed. *Shake.*

Dissolve the zinc sulphate in 60 cc. and the lead acetate in 30 cc. of water. Mix the two solutions gradually with shaking. Then add the tinctures in order, and finally rinse the graduate with the remaining 10 cc. of water.

85

- R. Acid sulphurici,
Acid nitrici..... aa 5.0
Olei terebinthinæ..... 15.0
Alcohol..... 25.0
M. Ft. lotio.

Place the oil in a capacious porcelain capsule or mortar, under a hood or out of doors. Mix the acids and slowly add to the oil at arm's length. When the reaction is over and mixture has cooled, add the alcohol and bottle.

(This is liable to take fire if the acids are added too fast.)

86

- R. Acid nitric,
Chloroformi,
Creosoti..... aa 5
M.

Mix the nitric acid and creosote in an open dish under the hood or in the open air, and when reaction has ceased and the mixture cooled add the chloroform.

87

- R. Ferrous sulphate, in clear
crystals..... 6 Gm.
Myrrh, in small pieces.... 18 Gm.
Sugar..... 18 Gm.
Potassium carbonate..... 8 Gm.
Spirit of lavender..... 60 cc.
Rose water, a sufficient
quantity to make.... 1000 cc.
M. Sig.—Griffith's mixture.

"Rub the myrrh, sugar, and potassium carbonate in a mortar, with 700 cc. of rose water, at first very gradually added, so that a uniform mixture may result. Transfer this to a graduated vessel, add the spirit of lavender, then the ferrous sulphate, previously dissolved in about 50 cc. of rose water, and lastly, enough rose water to make the product measure 1000 cc. Mix the whole thoroughly. This preparation should be freshly made, when wanted."

Make four fluidounces of the mixture. (This mixture, *without the iron*, keeps well, and is frequently so prepared in quantity. When required for use, 3 grains of granulated sulphate of iron are added to each ounce of mixture and well shaken for a few moments.)

88

- R. Potassæ sulphuratæ,
Zinci sulphatis..... aa 3 j
Ætheris,
Alcoholis..... aa 3 x
Aquæ rosæ..... 3 iss
M. Ft. lotio.

Dissolve the salts separately in 3vj of rose water, mix with stirring, and add the alcohol and ether. Dispense with a shake-label.

80

- R. Bismuthi et ammonii citratis 3 iij
 Acidi nitrici diluti. q. s.
 Aquæ. ad. 3 iv
 M. Sig.—Teaspoonful as directed.

On adding diluted nitric acid to the bismuth salt, previously dissolved in the water, bismuth citrate is precipitated in a very fine gelatinous condition, which remains suspended for a long time. An excess of acid should be avoided—better a slight deficiency than an excess. In the above the salt may be dissolved in 2 1/2 fluidounces of water, and 19 drachms of this precipitated with diluted nitric acid, then the remainder of the solution added. From 4 to 5 drachms of acid are required.

90

- R. Bismuthi subnit. 4.0
 Tragacanthæ pulv. 1.3
 Alcoholis. 8.0
 Aquæ cinnamomi. ad. 120.0
 M. Sig.—Bismuth mixture.

Place the tragacanth in a dry bottle or mortar, add the alcohol, mix well, then add 50 cc. of cinnamon water, mix thoroughly and add the bismuth and the rest of the cinnamon water.

Make also without the tragacanth and alcohol.

91

- R. Ferri et potassii tartratis. . . 4.0
 Potassii bromidi. 4.0
 Syrupi. 15.0
 Aquæ destillatæ. ad. 60.0
 M.

The first two ingredients are incompatible. Dissolve the iron salt in 25 cc. of water and add the syrup. Dissolve the bromid in the remainder of the water and mix with the iron solution. This begins to precipitate after standing an hour (or less), but the decomposition is less rapid than if the two salts are placed together in the bottle.

92

- R. Pulv. camphoræ. gr. xv
 Sodii boratis. gr. x
 Alcoholis. 3 ss
 Aquæ rosæ. 3 iiiss
 M. Ft. lotio.

Dissolve the camphor in the alcohol and the borax in the rose water.

Add the first solution to the second, and dispense with a shake-label.

93

- R. Aquæ ammoniæ. 60 cc.
 Spiritus camphoræ. 10 cc.
 Sodii chloridi. 60 Gm.
 Aquæ. ad. 1000 cc.

Dissolve the salt in about 900 cc. of water, add the ammonia and the camphor, and enough water to make 1000 cc. *Shake*.

Make six fluidounces.

- M. Sig.—“Sedative water.”

94

- R. Tinct. benzoini. 10.0
 Aquæ destillatæ. 150.0
 M. Sig.—“Lac Virginis.”

Pour the tincture slowly into the water, with constant shaking. This is used (diluted with water) as a toilet wash, and gum should not be used for emulsifying it. If the tincture is added slowly, a milky mixture results.

95

- R. Potassii chloratis..... $\frac{3}{4}$ j
 Tinct. opii camphoratae... $\frac{3}{4}$ iv
 Tinct. benzoini comp..... $\frac{3}{4}$ iiss
 Syrupi tolutani..... $\frac{3}{4}$ j
 Aquam.....ad. $\frac{3}{4}$ iv

M. Ft. garg.

Dissolve the potassium chlorate in two ounces of water. Mix $\frac{3}{4}$ ij of mucilage of acacia with the syrup, and gradually add the comp. tincture of benzoin with constant stirring. Then add the aqueous solution, and lastly the paregoric.

96

- R. Potassii chloratis..... gr. xv
 Tinct. cinchonae comp.,
 Tinct. guaiaci..... aa $\frac{3}{4}$ iiss
 Mellis..... $\frac{3}{4}$ j
 Aquae menthae piperitae ad. $\frac{3}{4}$ iv

M. Ft. garg.

Honey suspends resins better than syrup. The guaiac tincture should be added last and *very slowly*, with constant stirring.

97

- R. Sodium bicarbonate.... 35 Gm
 Fluidextract of rhubarb . 15 cc.
 Fluidextract of ipecac... 3 cc.
 Glycerin..... 200 cc.
 Spirit of peppermint.... 35 cc.
 Water, a sufficient quantity to make..... 1000 cc.

M. Sig.—Rhubarb and soda mixture.

Dissolve the sodium bicarbonate in about 400 cc. of water. Then add the fluid extracts, the glycerin, and the spirit of peppermint, and lastly, enough water to make 1000 cc.

Make 4 fluidounces.

98

- R. Fluidextract of glycyrrhiza..... 120.00 cc.
 Antimony and
 potassium tartrate 0.24 Gm.
 Camphorated tincture
 of opium..... 120.00 cc.
 Spirit of ethyl nitrite 30.00 cc.
 Glycerin..... 120.00 cc.
 Water, a sufficient quantity to make. 1000.00 cc.

M. Sig.—Brown mixture.

Mix the fluidextract of glycyrrhiza, with 500 cc. of water and the glycerin. Add the tartar emetic dissolved in 12 cc. of hot water, then the other ingredients and enough water to make 1000 cc.

99

- R. Saponis hispan..... $\frac{3}{4}$ iv
 Sodii carbonat..... $\frac{3}{4}$ ij
 Sodii boratis..... $\frac{3}{4}$ j
 Aquae ammoniae..... $\frac{3}{4}$ viij
 Alcoholis..... $\frac{3}{4}$ iiij
 Aetheris..... $\frac{3}{4}$ ij
 Aquae.....ad. Cong. j

M. Ft. solut. Sig.—Cleansing fluid.

100

- R. Quininae sulph..... 2.0
 Ext. glycyrrhiz. fld..... 10.0
 Syr. zingiberis..... 20.0
 Aquae..... 30.0

M. Sig.— $\frac{3}{4}$ j ante cibum.

101

- R. Prepared chalk..... 6 Gm.
 Glycerin..... 10 cc.
 Cinnamon water..... 40 cc.
 Distilled water, to make 100 cc.

Sig.—Chalk mixture.

Rub the chalk in a mortar, with the glycerin to a uniform mixture and add the cinnamon water. Transfer the mixture to a graduated flask, and rinse the mortar with enough water to make the product measure 100 cc. Mix the whole thoroughly. This preparation should be freshly made when wanted.

102

- R. Chloralis..... ʒ j Pulverize the camphor and triturate
 Camphoræ..... gr. xv with the syrup. Dissolve the chloral in
 Syr. zingiberis..... ʒ ss the water and mix the two liquids. Do
 Aquæ..... ʒ iss not triturate the chloral and camphor
 M. together.

103

- R. Pulv. rhei..... ʒ j Triturate the solids lightly with the
 Pulv. cinnamomi..... ʒ ij water gradually added.
 Magnesiae..... ʒ ij
 Aquæ..... ʒ iv
 M. Sig.—Rhubarb and magnesia
 mixture.

104

- R. Salolis..... ʒ j Salol is not easily powdered by trit-
 Mucilaginis tragacanthæ.... ʒ ij uration, adhering to the pestle and
 Aquæ..... ʒ iv sides of the mortar when rubbed. By
 M. dissolving the salol in alcohol, adding
 ʒij of powdered tragacanth and trit-
 urating with enough water to make
 4 ounces, a presentable mixture is
 easily obtained.

105

- R. Zinci oxidi..... ʒ ij Triturate the zinc oxid to a smooth
 Spiritus camphoræ..... ʒ iij paste with the glycerin, add the water,
 Liq. plumbi subacet..... ʒ iss and lastly, the camphor and lead
 Glycerini..... ʒ ss solution.
 Aquæ..... ʒ viij
 M. Ft. lotio. Sig.—“For local use
 —shake.”

106

- R. Iodoformi..... 3 Mix the glycerin and half of the water
 Amyli..... i and heat to 120° C. Mix the dry starch
 Glycerini..... 20 with the rest of the water and add to the
 Aquæ..... 12 hot mixture. Continue the heat until
 M. Ft. enema. Sig.—Inject as the starch is gelatinized, cool and
 directed. incorporate the iodoform.

107

- R. Sodii salicylat..... ʒ vi Sodium bicarbonate, being less soluble
 Potass. bicarbonat..... ʒ viii than potassium bicarbonate, forms
 Elix lactopeptin..... ʒ iss slowly and crystallizes out.
 Aquæ..... ʒ iv

108

- R. Sulphuris praecip..... ʒ iv Triturate the precipitated sulphur
 Aquæ rosæ..... ʒ iv with 15 grains of powdered orris root,
 M. Ft. lotio. then gradually add the rose water.

E. Decoctions and Infusions

109

- R. Wild cherry, in No. 20 “Moisten the powder with 60 cc.
 powder..... 40 Gm. of water, and macerate for one hour;
 Water, a sufficient quan- then pack it firmly in a conical glass
 tity to make..... 1000 cc. percolator, and gradually pour water
 M. Sig.—Infusion of wild cherry. upon it until the infusion measures
 1000 cc.”
 Make four fluidounces.

110

- R. Cinchona, in No. 40 powder..... 60 Gm.
 Aromatic sulphuric acid 10 cc.
 Water, a sufficient quantity to make..... 1000 cc.
- M. Sig.—Infusion of cinchona.
 Make four fluidounces.

Mix the acid with 500 cc. of water, and moisten the powder with 30 cc. of the mixture; pack it firmly in a conical glass percolator, and gradually pour upon it, first, the remainder of the mixture, and afterward water until the infusion measures 1000 cc.

111

- R. Digitalis, bruised..... 15 Gm.
 Alcohol..... 100 cc.
 Cinnamon water..... 150 cc.
 Boiling water..... 700 cc.
 Cold water, a sufficient quantity to make... 1000 cc.
- M. Sig.—Infusion of digitalis.

Upon the digitalis, obtained in a suitable vessel, pour the boiling water and allow it to macerate one hour. Then filter, add the alcohol and cinnamon water to the filtrate, and pass enough cold water through the residue on the filter to make the product measure 1000 cc.

Make 100 cc.

112

- R. Senna..... 60 Gm.
 Manna..... 120 Gm.
 Magnesium sulphate... 120 Gm.
 Fennel, bruised..... 20 Gm.
 Boiling water..... 800 cc.
 Cold water, a sufficient quantity to make... 1000 cc.
- M. Sig.—Black draught.

Upon the senna and fennel, contained in a suitable vessel, pour the boiling water and macerate half an hour. Then strain with expression, dissolve in the infusion the magnesium sulphate and manna, and again strain. Lastly, add enough cold water through the strainer containing the senna and fennel to make the infusion measure 1000 cc.

Make four fluidounces.

113

- R. Sarsaparilla, cut and bruised..... 100 Gm.
 Sassafras, in No. 20 powder..... 20 Gm.
 Guaiacum wood, rasped. 20 Gm.
 Glycyrrhiza, bruised... 20 Gm.
 Mezereum, cut and bruised..... 10 Gm.
 Water, a sufficient quantity to make..... 1000 cc.
- M. Sig.—Compound decoction of sarsaparilla.

Boil the sarsaparilla and guaiacum wood for half an hour in a suitable vessel with 1000 cc. of water. Then add the sassafras, glycyrrhiza, and mezereum, cover the vessel well, and macerate for two hours. Finally strain, and add enough cold water, through the strainer, to make the product measure 1000 cc.

Make three fluidounces.

114

- R. Acidi benzoici,
 Sodii boratis..... aa 3 ij
 Infusi buchu..... 3 vj
- M. Sig.—Dessertspoonful in half a glass of water every three hours.

115

- R. Quillajæ..... 3 iv
 Rosæ Gallicæ..... 3 ij
 Fiat infusum..... 3 viij et adde
 Saponis..... 3 j
 Alcoholis..... 3 iv
 Glycerini..... 3 vj
 Mentholi..... gr. j
 Thymoli..... gr. ss
 Olei aurantii.... gtt. x
 Olei cinnamomi... gtt. iij
 Olei gaultheriæ... gtt. xv
- M. s. a. Sig.—Toothwash.

116

- R. Chondri..... gr. lxxij
 Aquæ..... ʒ vj
 M. Fiat mucilago. Sig.—Mucilage
 of Irish moss.

Select the moss, wash it with cold water, then place it in a capacious vessel, add 6 fluidounces of water, and apply heat until the water has boiled gently for 15 minutes. Then strain, and add enough water through the strainer to make the liquid measure, when cold, 6 fluidounces. If boiled in an open dish, water must be added from time to time to supply that lost by evaporation.

117

- R. Chondri..... ʒ j
 Glycerini..... ʒ iss
 Aquæ q. s. ut. ft..... ʒ viij
 M. s. a.

Wash the moss with water, then place in a suitable dish and pour upon it a quart of water. Apply heat and boil until the whole is reduced to about 6 fluidounces. Strain while hot, add the glycerin, and pass enough water through the strainer to make 8 fluidounces. (If bottled immediately this keeps well.)

118

- R. Chondri..... 2.0
 Aquæ destillatæ..... 75.0
 Misce coque et cola, denique
 adde,
 Aquæ bullientis..... ad. 75
 Glycerini..... 30
 Alcoholis..... 15
 M. Sig.—Permanent mucilage of Irish
 moss.

Select the Irish moss and boil half an hour in a capacious vessel, being careful not to scorch nor to allow to boil over. Keep up the volume with hot water while boiling.

Prescriptions from State Board Examinations

For criticism, suitability for compounding, methods of mixing, translation into other metrological systems, and practice.

1

- R. Acetanilidi..... ʒ i
 Cod. sulph..... gr. iv
 Caf. citrat..... gr. xxx
 Elix. simp..... ʒ ii
 Syr. prun. virg..... ʒ i
 M. Ft. sol. Sig.—A teaspoonful for
 headache. (Tex.)

3

- R. Sodii citrat..... 45.00
 Hexamethylen..... 15.00
 Aquæ dest..... 75.00
 Aquæ menth. pip..... ad. 180.00
 M. Sig.—ʒii in one-half glass of
 water every three hours. (Pa.)

5

- R. Potassii chloratis..... ʒ ii
 Syr. ferri iodidi..... ʒ iv
 Vini antimonii..... ʒ ss
 Aquæ..... ad. ʒ vi
 M. Sig.—Teaspoonful every three
 hours. (Ill.)

2

- R. Morphinae sulph..... 0.25
 Aquæ..... 0.10
 Zinci sulph..... 12.00
 M. Ft. solut. Sig.—Use as injec-
 tion. (Ark.)

4

- R. Tinct. ferri chlorid..... ʒ ii
 Tinct. cinchonæ..... ʒ iv
 Glycerini..... ʒ iv
 Aquæ..... q. s. ad. ʒ iii
 M. Sig.—Teaspoonful t. i. d. (Ill.)

6

- R. Ferri et quiniæ cit..... ʒ i
 Ammon. chlorid..... ʒ ii
 Fldest. glycyrrhiz..... ʒ iv
 Aquæ..... q. s. ad. ʒ iv
 M. Sig.—A teaspoonful every three
 hours. (Ind.)

7

- R. Quininae sulph. 1.00
 Ammon. carb. 3.00
 Alcohol. 25.00
 Elixir. 50.00
 Aquæ. ad. 100.00
 M. Ft. mist. s.a. Sig.—A teaspoonful in water every three hours. (Wash.)

9

- R. Potass. citrat
 Potass. acetat. āā 3 iv
 Tinct. belladonnæ. 3 v
 Elixir simpl. ad. 3 iv
 M. Sig.—Teaspoonful three times a day. (Wash.)

11

- R. Quininae sulph. 1.0
 Acidi sulphurici dil. q.s.
 Syrupi. 30.0
 Aquæ. ad. 60.0
 M. Sig.—Teaspoonful every two hours. (N. Y.)

13

- R. Cretæ præparat. 3 iss
 Tinct. opii deod. ℥ xx
 Tinct. kino. 3 iv
 Mucil. acaciæ. 3 iv
 Aquæ cinnamomi. ad. 3 iv
 M. Sig.—3 i q. q. bis aut tres horas. (S. D.)

15

- R. Thymol. ʒ i
 Magnes. carb. levis. gr.v
 Spir. chloroformi,
 Tinct. benzoini co. āā 3 iii
 Aquæ. ad. 3 ii
 M. Ft. vapor. (Br. Col.)

17

- R. Potass. iodid. 3 iiss
 Ammon. chlor. 3 iss
 Tinct. opii camph. 3 iv
 Syr. pruni virg. 3 iii
 Aq. chloroformi. ad. 3 viii
 M. (Br. Col.)

19

- R. Tinct. ferri chlor. 3 ii
 Potass. chlor. 3 i
 Glyc. acid tannic. 3 iv
 Aquæ. ad. 3 iv
 M. Ft. garg. (Br. Col.)

8

- R. Arseni trioxidi. 1.00
 Acid hydrochlor. dil. 5.00
 Aquæ destillat. ad. 100.00
 M. Ft. solut. Sig.—Solution of arsenous acid. (Wash.)

10

- R. Spir. æth. nitros. 3 ii
 Antipyrini. 3 ss
 Syrupi. 3 iv
 Aquæ. ad. 3 ii
 M. Sig.—Teaspoonful p. r. n. (N. Y.)

12

- R. Tinct. cinchon. comp. 3 iv
 Spir. ammon. arom. 3 ii
 Glycerini. 3 ss
 Aquæ. ad. 3 iii
 M. Sig.—3 i every three hours. (Mass.)

14

- R. Chrysarobini. 2.6
 Resorcinoli. 0.78
 Traumaticini. 30.00
 Misce ft. mistura.
 Sig.—Agitato vase, admoveatur bis in die. (Tenn.)

16

- R. Ung. hydrarg. 3 i
 Liq. ammon. fort. ℥ clx
 Linim camph. ad 3 iii
 M. Ft. linim. (Br. Col.)

18

- R. Hydrarg. subchlor. gr. xxx
 Glycerini. 3 iv
 Mucil. tragac. 3 x
 Liq. calcis. ad. 3 x
 M. Ft. lotio. (Br. Col.)

20

- R. Bismuthi subcarb. 3 ii
 Pepsini. ʒ ii
 Acid mur. dil. 3 ii
 Fldext. nuc. vom. 3 i
 Aq. menth. pip. ad. 3 iv
 M. Sig.—3 ss three times a day. (Br. Col.)

21

R. Bismuthi subnit.....	4.00
Pulv. tragacanth.....	1.30
Alcoholis.....	8.00
Aquæ.....ad.	120.00
M. (Ill.)	

23

R. Ol. sassafras.....	℥ vii
Tinct. tolu.....	℥ i
Magnes. carb.....	℥ ii
Morphinæ sulph.....	gr. viii
Sacchari alb.....	℥ xxii
Aquæ dest.....	O i
M. Ft. syr. s. a. (Tenn.)	

25

R. Sol. cocaine mur., 7 percent	℥ i.
M. Sig.—Local use. (Fla.)	

27

R. Arseni trioxidi.....	gr. i
Tinct. ferri chlor.....	℥ iv
Strychninæ sulph.....	gr. i
Acid muriat dil.....	℥ iii
Syr. simplicis.....ad.	℥ vi
M. Sig.—℥ i in aq. t. i. d. p. c. (Fla.)	

29

R. Bismuthi subnit.....	4.00
Pulv. tragacanthæ.....	1.30
Tinct. nucis vom.....	8.00
Aquæ.....q. s. ut. ft.	120.00
M. s. a. Sig.—℥ i t. i. d. (Ill.)	

31

R. Quininæ sulph.....	gr. xx
Potass. iodidi.....	℥ i
Elixir aromat.....	℥ iii
Aquæ dest.....	℥ iii
M. Sig.—Teaspoonful three times a day. (N. J.)	

33

R. Tinct. aconiti.....	℥ xxx
Strychninæ sulph.....	gr. ss
Quinin. sulph.....	gr. xl
Ac. sulph. dil.....	℥ i
Elix. simp.....	℥ iv
Aquæ.....ad.	℥ iv
M. Sig.—Teaspoonful every three hours. (N. J.)	

22

R. Phenoli.....	℥ ii
Liq. calcis.....	℥ xiv
M. Sig.—Apply on gauze to affected parts. (Tenn.)	

24

R. Potass. chloratis.....	℥ i
Acid hydrochlor.....	℥ i
Glycerini.....	℥ iv
Aquæ destil.....	℥ iiiiss
M. Ft. sol. (Tenn.)	

26

R. Bismuthi subnit.....	gr. xvi
Hydrarg c cretæ.....	gr. xvi
Tr. opii camph.....	℥ ii
Aquæ menth. pip.....ad.	℥ ii
M. Sig.—Teaspoonful every two or three hours for bowels. (Fla.)	

28

R. Sol. hydrarg. bichlor.....	℥ iv
(Make of such strength that when ℥ i is added to a quart of water a solution containing 1 to 3000 will be obtained.)	(Fla.)

30

R. Sodii salicylat.....	℥ i
Glycerini.....	℥ iss
Ol. gaulther.....	℥ i
Tinct. ferri chlor.....	℥ iss
Acid citrici.....	gr. v
Spir ammon. arom.....ad.	℥ ii
M. Sig.—One dessertspoonful two or three times a day. (Wis.)	

32

R. Hydrarg. chlor. corros.....	gr. iii
Potass. iodid.....	℥ iii
Tinct. cinchonæ comp.....	℥ iii
Aquæ dest.....	℥ iii
M. Ft. sol. Sig.—A teaspoonful every three or four hours. (N. J.)	

34

R. Ammon. chlor.....	2.00
Terpini hydrat.....	1.00
Fldext. grindeliæ.....	4.00
Syr. pruni virg.....	15.00
Aquæ.....ad.	30.00
M. Sig.—4 cc. t. i. d. (N. Y.)	

35

- R. Potassii chloratis..... 1.0
 Syr. ferri iodidi..... 3.0
 Spir. chloroformi..... 1.0
 Aquæ menth. pip.....ad. 30.0
 M. (N. Y.)

37

- R. Liq. plumbi subacetat..... 1.0
 Zinci sulphat..... 0.5
 Tinct. catechu..... 1.0
 Tinct. opii..... 1.0
 Aquæ.....ad. 60.0
 M. (N. Y.)

39

- R. Magnesii sulphat..... $\frac{3}{4}$ i
 Tinct. zingiberis..... $\frac{3}{4}$ i
 Tinct. aurant. dulc..... $\frac{3}{4}$ i
 Aquæ menth. pip..... $\frac{3}{4}$ ii
 M. Sig.—A tablespoonful before
 breakfast. (Col.)

41

- R. Ammon. carb..... gr. xxiv
 Ammon. chlor..... gr. xxx
 Syr. scillæ..... $\frac{3}{4}$ i
 Aquæ.....ad. $\frac{3}{4}$ ii
 M. (Ga.)

43

- R. Tr. opii camph.,
 Syr. zingiberis,
 Aquæ.....aa $\frac{3}{4}$ i
 M. Sig.—One teaspoonful every four
 hours. (Wash.)

45

- R. Tinct. ferri chlor..... $\frac{3}{4}$ ii
 Spir. eth. nit..... $\frac{3}{4}$ ii
 Mucil. acaciæ..... $\frac{3}{4}$ i
 Syrupi..... $\frac{3}{4}$ x
 M. (State order of mixing.) (Ill.)

47

- R. Tinct. ferri chlor..... $\frac{3}{4}$ ii
 Infus. uvæ ursi..... $\frac{3}{4}$ v
 Syrupi.....ad. $\frac{3}{4}$ vi
 M. Sig.—Tablespoonful every three
 hours. (Ind.)

49

- R. Aquæ ammon..... 35.0
 Alcoholis..... 5.0
 Olei gossypii..... 57.0
 Acid oleic..... 3.0
 M. Sig.—Liniment. (Col.)

36

- R. Hydrarg. bichlorid..... 1.0
 Potass. iodidi..... 4.0
 Tr. cinchon..... 30.0
 Syrupi..... 30.0
 M. Sig.—A teaspoonful every three
 hours. (N. Y.)

38

- R. Sodii phosphat..... 10.0
 Sodii nitratiss..... 0.4
 Acidi citrici..... 1.3
 Aquæ dest.....ad. 100.0
 M. Ft. sol. (N. Y.)

40

- R. Tinct. ferri chlor..... 4.0
 Acid acetic dil..... 6.0
 Liq. ammon. acet..... 50.0
 Elixir aromat.,
 Glycerini.....aa 12.0
 Aquæ.....ad. 100.0
 M. Sig.—8 cc. every four hours.
 (Col.)

42

- R. Quininae sulphat..... gr. xvi
 Acidi tannici..... gr. xxx
 Acid sulphurici dil..... $\frac{3}{4}$ ii
 Aquæ.....q. s. ad. $\frac{3}{4}$ ii
 M. Sig.—Teaspoonful three times a
 day. (Ind.)

44

- R. Liq. potass. arsenit..... $\frac{3}{4}$ iss
 Ferri et ammon. cit..... $\frac{3}{4}$ iiss
 Tinct. calumbæ..... $\frac{3}{4}$ vi
 Aquæ.....ad. $\frac{3}{4}$ iv
 M. Sig.—Teaspoonful in water after
 meals. (Wash.)

46

- R. Potass. iodidi..... gr. lx
 Syr. ferri iodid..... $\frac{3}{4}$ iv
 Infus. calumbæ.....ad. $\frac{3}{4}$ iv
 M. Sig.—Teaspoonful every two
 hours. (Ind.)

48

- R. Chloral hydrat..... $\frac{3}{4}$ iv
 Camphoræ..... $\frac{3}{4}$ iv
 Olei terebinth.,
 Tinct. capsici.....aa $\frac{3}{4}$ ii
 Linim. chloroformi.....ad. $\frac{3}{4}$ v
 M. Sig.—Liniment. (Col.)

50

- R. Calcii lactatis..... $\frac{3}{4}$ i
 Potass. citratis..... gr. xl
 Elixir aromat..... $\frac{3}{4}$ ii
 M. Sig.—Teaspoonful after each
 meal. (Mass.)

51

- R. Phenol..... gr. x
 Tinct. myrrhæ..... $\overline{3}$ ii
 Potass. chlorat..... gr. xxx
 Aquæ..... q. s. ut. ft. $\overline{3}$ iv
 M. Sig.—Gargle t. i. d. (Tex.)

52

- R. Ammon. carb..... $\overline{3}$ ii
 Sp. eth. nit..... $\overline{3}$ ii
 Syr. scillæ..... $\overline{3}$ iv
 Sry. tolut..... ad. $\overline{3}$ iv
 M. Ft. solut. Sig.—Coch. parv.
 (Tex.)

53

- R. Liq. potass. arsenit..... $\overline{3}$ iss
 Ferri et ammon. cit..... $\overline{3}$ iiss
 Tinct. calumb..... $\overline{3}$ vi
 Aquæ..... ad. $\overline{3}$ iv
 M. Sig.—A teaspoonful in water
 after meals. (Minn.)

54

- R. Acidi salicylici..... 8.5
 Potass. citratis..... 12.5
 Glycerini..... 50.0
 Elixir arom..... ad. 100.0
 M. et ft. solut. (Mass.)

55

- R. Hydrarg. chlor. corros.... gr. xvi
 Collodii..... $\overline{3}$ iv
 M. Sig.—Apply as directed with a
 brush. (Mass.)

56

- R. Sol. hydrarg. chlor. corros.
 1 percent..... $\overline{3}$ iv
 M. Sig.—External use. Poison.
 (Mass.)

57

- R. Potass. bicarbonat..... 8.0
 Acidi citrici..... 6.0
 Aquæ..... ad. 100.0
 M. (N. Y.)

58

- R. Syr. scillæ..... $\overline{3}$ iii
 Vini ipecac..... $\overline{3}$ iv
 Tr. opii camph..... $\overline{3}$ ii
 Syr. tolut..... ad. $\overline{3}$ vi
 M. Sig.—Teaspoonful every four
 hours. (New Mex.)

59

- R. Spir. æth. nitros..... $\overline{3}$ iii
 Tinct. ferri chlor..... $\overline{3}$ iv
 Mucil. acaciæ..... $\overline{3}$ iss
 Glycerini..... $\overline{3}$ ii
 Syrupi..... ad. $\overline{3}$ vi
 M. Sig.—One dessertspoonful t. i. d.
 as directed. (Mass.)

60

- R. Tinct. ferri chlor..... $\overline{3}$ ii
 Potass. chlorat..... $\overline{3}$ i
 Aquæ dest..... ad. $\overline{3}$ vi
 M. Sig.—Gargle. Use one or two
 tablespoonfuls in a glass of water as
 directed. (Tex.)

61

- R. Cerii oxalat..... gr. xx
 Bismuthi subnit..... gr. xv
 Aquæ camph..... $\overline{3}$ i
 Ess. pepsin..... $\overline{3}$ iii
 M. Sig.— $\overline{3}$ ii in water every three
 hours. (Mucilage acacia q. s. to
 suspend.) (Pa.)

62

- R. Hydrarg. chlorid corros... 0.15
 Strychninæ sulph..... 0.05
 Chloral hydrat..... 8.00
 Tinct. ferri chlor..... 20.00
 Elix. adjuvantis..... ad. 125.00
 M. Sig.—One teaspoonful three
 times daily. (N. C.)

63

- R. Quininæ sulphat..... gr. xxx
 Plumbi acetatis..... gr. xl
 Bismuthi subnit..... $\overline{3}$ i
 Syr. zingiberis..... $\overline{3}$ iv
 M. Sig.—Teaspoonful every two
 hours. (N. C.)

64

- R. Takadiastase..... 10 percent.
 Tinct. nux vomic..... 10 percent.
 Ess. pepsin..... 50 percent.
 Tinct. gentian comp.. 30 percent.
 M. Mitte $\overline{3}$ iv. Sig.— $\overline{3}$ i ex aqua.
 p. c. (New Mex.)

65

- R. Potass. iodidi,
Fldest. trifol. comp.,
Fldest. taraxac.,
Syr. sarsap. comp. ad. $\mathfrak{z}$ iii
M. Ft. sol. Sig.—Coch. mag. omni
4 hora. (Fill in quantities for first
three ingredients, average adult
doses.) (New Mex.)

67

- R. Sodii bicarb. $\mathfrak{z}$ iii
Liq. potass. arsen. $\mathfrak{z}$ ii
Vini ferri. q. s. ut. ft. $\mathfrak{z}$ iii
M. Sig.— $\mathfrak{z}$ i in aq. t. i. d. p. c.
(N. C.)

69

- R. Ferri phosphat. solubilis. $\mathfrak{z}$ ss
Elixir aurantii. $\mathfrak{z}$ ii
M. Ft. sol. Sig.— $\mathfrak{z}$ i ante cib. in
H₂O. (Ill.)

71

- R. Hydrarg. bichlorid,
Kali iodidi,
Syrupi,
Aqua. aa q. s. $\mathfrak{z}$ iv
Fill in quantities for average and
maximum doses and dispense. (Wash.)

73

- R. Tinct. opii camph.
Syr. zingiberis.
Aqua. aa $\mathfrak{z}$ i
M. Sig.—One teaspoonful every four
hours. (Minn.)

75

- R. Quininæ sulph. 1.0
Ammon. carb. 3.0
Alcohol. 25.0
Elixir. 50.0
Aqua. ad. 100.0
M. Ft. mist. s. a. Sig.—A tea-
spoonful in water every three hours.
(Minn.)

77

- R. Ammonii chlorid. 1.0
Syrupi ipecacuanhæ. 10.0
Syrupi senegæ. 4.0
Misturæ glycyrrhiz comp. ad. 60.0
M. Sig.—A teaspoonful every three
hours. (N. Y.)

66

- R. Tinct. iodi,
Aqua ammon.,
Collodii. aa $\mathfrak{z}$ i
M. Sig.—Apply locally as directed.
(N. C.)

68

- R. Potass. brom. $\mathfrak{z}$ ii
Tinct. bellad. $\mathfrak{z}$ iv
Tinct. opii cam. $\mathfrak{z}$ vi
Syr. quin. ad. $\mathfrak{z}$ iii
M. Sig.— $\mathfrak{z}$ i q. three or four hours.
(N. C.)

70

- R. Acidi salicylici. $\mathfrak{z}$ ii
Ferri pyrophos. $\mathfrak{z}$ ss
Sodii phos. $\mathfrak{z}$ i
Aqua destillat. $\mathfrak{z}$ iii
M. et. ft. solut. Sig.—Dessertspoon-
ful every three hours in water.
(Ind.)

72

- R. Acid nitrohydrochloric. $\mathfrak{z}$ v
Ess. pepsin. $\mathfrak{z}$ ii
Aqua. ad. $\mathfrak{z}$ iii
M. Sig.—One teaspoonful before meals.
(Minn.)

74

- R. Acidi chromici. $\mathfrak{z}$ ss
Glycerini. $\mathfrak{z}$ ss
Alcoholis. $\mathfrak{z}$ iss
M. Apply externally with brush.
(N. Y.)

76

- R. Arseni trioxid. 1.0
Acid hydrochlor. dil. 5.0
Aqua destillat. ad. 100.0
M. Ft. solut. Sig.—Solution of
arsenous acid. (Minn.)

78

- For Judge William's little girl.
R. Kali citratis. $\mathfrak{z}$ iss
Spt. nit. dulcis. $\mathfrak{z}$ vi
Spt. mindererus. $\mathfrak{z}$ i
Syrupus tolu
Aq. dest. aa q. s. ad. $\mathfrak{z}$ vi
M. Sig.—Teaspoonful every three
hours. (Tex.)

79

- R. Cretæ præparat. ʒ iss
 Tinct. opii deod. ℥ xx
 Tinct. kino. ʒ ss
 Mucil. acaciæ. ʒ iv
 Aquæ cinnamomi. ad. ʒ iv
 M. Sig.—ʒ i q. q. bis. aut tres horas.
 (Tex.)

81

- R. Hydrarg. bichlorid. gr. iii
 Potass. iodidi. ʒ ii
 Syr. ferri iodid. ʒ i
 Aquæ dest. ʒ i
 Syrupi. ad. ʒ vi
 M. Ft. sol. Sig.—As directed.
 (How much bichloride of mercury in
 each cc. of this mixture?) (Mo.)

83

- R. Acid nitromuriat. ʒ ii
 Tinct. nucis vom. ʒ i
 Tinct. card. co. ʒ ii
 Tinct. gentianæ co. ad. ʒ iv
 M. Sig.—One teaspoonful after meals.
 (Mass.)

85

- R. Syr. scillæ. ʒ iii
 Vini ipecac. ʒ iv
 Tinct. opii camph. ʒ ii
 Syr. tolut. ad. ʒ vi
 M. Sig.—Teaspoonful every four
 hours. (Mont.)

87

- R. Potass. chloratis. ʒ iv
 Tinct. myrrhæ. ʒ iv
 Fl̄dext. hydrastis. ʒ ii
 Aquæ. ad. ʒ iv
 M. Sig.—Use as gargle. (Ala.)

89

- R. Zinci oxid. ʒ ii
 Spir. camphoræ. ʒ iii
 Liq. plumbi subacet. ʒ iss
 Glycerini. ʒ ss
 Aquæ. ad. ʒ viii
 M. Ft. lotio. Sig.—External use.
 (Mass.)

91

- R. Zinci sulphat. gr. iii
 Cocainæ mur. gr. i
 Glycerini. ʒ ss
 Sol. corrosiv. (1:10,000) ad. ʒ i
 M. Ft. collyr. Sig.—Drop in eye
 as directed. (Wis.)

80

- R. Potass. chloratis. gr. x
 Acidi hydrochlorici. ℥ x
 Syrupi aurantii. ʒ i
 Aquæ destillatæ. ad. ʒ viii
 M. Ft. solut. sec. art. Sig.—Half
 tablespoonful every four hours.
 (Mo.)

82

- R. Zinci sulph. gr. iii
 Cocainæ mur. gr. i
 Glycerini. ʒ ss
 Sol. corrosive (1:10,000) ad. ʒ i
 M. Sig.—Drop in eye as directed.
 (N. H.)

84

- R. Ferri sulphat. 3.00
 Myrrhæ. 9.00
 Sacchari. 9.00
 Potass. carb. 4.00
 Sp. lavandulæ. 30.00
 Aquæ rosæ. ad. 500.0
 M. s. a. (Okla.)

86

- R. Morphinæ sulph. gr. xii
 Acid borici.
 Sodii boratis. āā gr. v
 Aquæ destillat. ʒ i
 M. Ft. collyr. Sig.—Drop into eye
 several times daily. (Neb.)

88

- R. Tinct. cinchon comp. ʒ ss
 Spir. ammon. arom. ʒ ii
 Glycerini. ʒ iv
 Aquæ. q. s. ad. ʒ iii
 M. Sig.—ʒ i every three hours.
 (N. Y.)

90

- R. Tinct. benz. co. ʒ i
 Mentholi. gr. x
 Chloroformi. ʒ iv
 M. Sig.—One or two teaspoonfuls
 in a cup of hot water for inhala-
 tion. (Ill.)

92

- R. Atropinæ sulph. gr. i
 Cocainæ mur. gr. ii
 Sodii boratis. gr. vi
 Aquæ dest. ad. ʒ i
 M. Ft. collyr. Sig.—One or two
 drops in eye t. i. d. (Wis.)

93

- R. Tinct. ferri chlor. ʒ iv
 Spiritus vini rect. ʒ iv
 Mucilaginis acaciæ. ʒ ii
 Syrupi. q. s. ut. ft. ʒ iv
 M. (Ill.)

95

- R. Plumbi acet. ʒ i
 Tinct. opii. ʒ ii
 Aquæ. ad. ʒ vi
 M. s. a. Sig.—Lotion. (N. Y.)

97

- R. Sol. hydrarg. chlor. corros.
 1:5000 in physiological sol. O i
 (Ill.)

99

- R. Hydrarg. submur. gr. xxx
 Mucil. tragacanthæ. ʒ i
 Liquoris calcis ad. ʒ viii
 M. Sig.—Apply twice a day. (Fla.)

101

- R. Quinina sulph. ʒ i
 Tinct. nucis vom. ʒ i
 Spir. ammon arom. ʒ ii
 Syr. aurant. ʒ vi
 Aquæ. q. s. ad. ʒ vi
 M. Sig.—Teaspoonful t. i. d. p. c.
 (Fla.)

103

- R. Potass. iodid. ʒ iv
 Strych. sulph. gr. i
 Tinct. digitalis. ʒ iv
 Tinct. ferri chlor. ʒ iv
 Tinct. cinchon. co. ad. ʒ iv
 M. Sig.—One teaspoonful t. i. d.
 (N. C.)

105

- R. Spir. æth nit. ʒ vi
 Fldext. buchu. ʒ iv
 Fldext. uvæ ursi. ʒ iv
 Syrupi. q. s. ad. ʒ iv
 M. Sig.—Teaspoonful 4 times a day
 (N. C.)

94

- R. Acidi salicylici. 8.0
 Natrii bicarb. 5.8
 Glycerini. 20.0
 Aquæ. ad. 60.0
 M. s. a. Sig.—Teaspoonful in water
 four times a day. (N. Y.)

96

- R. Ammon. chlorid. 2.00
 Terpinii hydrat. 3.00
 Fldext. buchu. 4.00
 Aquæ. ad. 30.00
 M. Sig.—ʒi three times a day. (Vt.)

98

- R. Zinci sulphatis
 Potass. sulphurat. āā 3.0
 Aquæ rosæ. 50.0
 M. Ft. lotio. Sig.—Applicandum
 p. r. n. (N. C.—N. Y.)

100

- R. Bismuthi subnit. ʒ vi
 Liq. aromat. alkal. ʒ v
 Zinci sulphocarb. ʒ ii
 Tinct. opii deod. ʒ iv
 Ess. pepsin. ad. ʒ iv
 M. Sig.—ʒ ii in water every 3 hrs.
 (N. C.)

102

- R. Tinct. digitalis. ʒ vi
 Tinct. ferri chlor. ʒ iv
 Elix. lactat pepsin. ad. ʒ ii
 M. Sig.—ʒi in water every 4 hrs.
 (N. C.)

104

- R. Potass. chlorat. gr. xv
 Spir. æth nit. ʒ iss
 Tinct. guaiaci. ʒ i
 Glycerini. ʒ iv
 Aq. destillat. ad. ʒ ii
 M. Sig.—Coch. parv. omni hora.
 (No. Dak.)

106

- R. Liq. arsen. et hydrarg iod. ... ʒ i
 Tinct. nucis vom. ʒ v
 Tinct. ferri chlor. ʒ vi
 Tinct. cinchonæ co. ad. ʒ iv
 M. Sig.—Teaspoonful p. c. (N. C.)

107

- R. Quininæ sulphat. gr. xxx
 Liq. ferri et ammon acet. 3 ii
 M. Sig.—Teaspoonful every 3 hrs.
 (N. C.)

109

- R. Tinct. ferri chlor. 5 ii
 Ammon. carbonat. q. s.
 Acidi acetici dil. 3 ii
 Glycerini. M. 3 ii
 M. (La.)

111

- R. Liq. fowleri. 5 iv
 Sodii bromidi. gr. xx
 Elix aromat. ad. 3 iii
 M. Sig.—3 ii t. i. d. (N. Y.)

113

- R. Sol. eserine sulph 0.25%... 3 i
 Sig.—One drop in eye night and
 morning. (Fla.)

115

- R. Acidi arsenosi. 3 ii
 Quininæ sulph. 3 ss
 Syr. sarsap. co. ad. 3 iv
 M. Sig.—Two teaspoonfuls 3 times a
 day. (Tex.)

117

- R. Hydrarg. submur. gr. xxx
 Glycerini. 3 ii
 Liq. calcii hydrox. ad. 3 viii
 M. Sig.—As directed. (Fla.)

119

- R. Zinci sulphatis
 Plumbi acetatis. aa gr. v
 Aquæ. 3 iv
 M. s. a. Sig.—Agita et utend ex modo
 præscripto. (Col.)

121

- R. Tinct. guaiaci ammon. 3 ii
 Tinct. opii deod. 3 iii
 Liquoris potassæ. 3 ii
 Aquæ cinnamomi. ad. 3 viii
 M. Sig.—Gargle every 2 hrs. (Wis.)

108

- R. Tinct. ferri chlor. 3 ii
 Tinct. gentianæ. 3 iv
 Aq. menth pip q. s. 3 iv
 M. Sig.—Teaspoonful in water after
 meals. (Tex.)

110

- R. Ammon carb. 2.5
 Tinct. ferri chlor. 4.0
 Glycerini. 12.0
 Elix. aromat. 12.0
 Acid acetic dil. 56.0
 Aquæ dest. ad. 100.0
 M. Ft. sol. (Col.)

112

- R. Tinct. aconiti. 3 i
 Spir. æth nitros. 3 i
 Syrupi. 3 i
 Liq. potass. cit. 3 iii
 M. Sig.—3 ss t. i. d. (Tex.)

114

- R. Strychninæ sulph. gr. i
 Tinct. nucis vomic
 Acid phosphorici dilut. aa 3 i
 Aquæ. ad. 3 iv
 M. Sig.—Teaspoonful 4 times a day.
 (Ind.)

116

- R. Magnesii sulphatis. 3 i
 Magnesii carbonatis. 3 ii
 Pulv. rhei. 3 ii
 Syrupi. 3 i
 Aq. menth. pip. ad. 3 viii
 M. Sig.—3 ss pro dosi omni mane
 (Br. Col.)

118

- R. Zinci sulphatis. gr. x
 Plumbi acetatis. gr. v
 Aquæ. 3 ii
 M. Sig.—Apply locally. (Mo.)

120

- R. Hydrarg. chlor. mit. 3 i
 Liquor calcis. 3 viii
 M. Sig.—Apply locally.

122

- R. Acidi salicylici. 2.00
 Sodii bicarbonatis q. s.
 Syrupi. 10.00
 Aquæ menth pip. ad. 60.00
 M. Sig.—Cochleare medium omni
 quarta hora. (N. Y.)

123

- R. Ammon carbonat..... 2
 Syrupi scillæ..... 20
 Syrupi ipecacuan..... 12
 Syrupi pruni virg ad..... 120
 M. Sig.—A teaspoonful every two hours.

125

- R. Tinct. myrrhæ..... ʒ ii
 Tinct. benzoini comp..... ʒ i
 Spir. camphoræ..... ʒ ii
 Aquæ rosæ..... ʒ iii
 M. Sig.—Use as mouth wash.
 (N. Y.)

127

- R. Phenolis..... gr. ii
 Mentholis..... gr. ii
 Cocainæ hydrochl..... gr. iv
 Petrolat. liquid..... ʒ i
 M. Ft. sol. Sig.—Use in atomizer.
 (Fla.)

129

- R. Solut. cupri sulphat 3 percent.
 Glycerini..... aa 15.0
 M. Ft. collyr. (N. Y.)

131

- R. Potass chlorat..... 2.0
 Tinct. myrrhæ..... 15.0
 Glycerini..... 30.0
 Aquæ..... ad. 120.0
 M. Ft. gargle. (La.)

133

- R. Sp. ætheris..... ʒ vi
 Chloroformi..... ʒ vi
 Aquæ ammoniæ..... ʒ iss
 M. Sig.—Liniment. (N. Y.)

135

- R. Acidi salicylici
 Sodii bicarbonat..... aa ʒ ss
 Caffeinæ citrat..... gr. xv
 Spir. æth. nit..... ʒ ss
 Aquæ..... ad. ʒ iii
 M. Sig.—ʒ i q. 4 hrs. (N. C.)

124

- R. Thymolis..... gr. v
 Mentholis..... gr. v
 Methylis salicylatis..... M xv
 Petrolati liq. levis..... ʒ i
 Aquæ creosoti..... ʒ ii
 M. Ft. nebul. Sig.—Use as spray.
 (N. Y.)

126

- R. Mentholis..... 1.00
 Chloroformi..... 4.00
 Tinct. benzoini..... 6.00
 Petrolati liquid..... 30.00
 M. Ft. solut. Sig.—Spray. (N. Y.)

128

- R. Liq. phenolis..... 1.5 per cent.
 Cocainæ hydrochlor 3.25 per cent.
 Aquæ..... q. s. ad. ʒ iss
 M. Sig.—For local use. (Fla.)

130

- R. Tinct. benzoini
 Tinct. myrrhæ..... aa ʒ ss
 Aquæ rosæ..... ʒ iii
 M. Sig.—Mouth wash. (N. Y.)

132

- R. Tinct. capsici..... ʒ iv
 Ol betulæ..... ʒ iv
 Aquæ ammoniæ..... ʒ iss
 Alcoholis..... ad. ʒ iv
 M. Sig.—Liniment. (Wash.)

134

- R. Sodii salicylat..... ʒ ii
 Syr. acidi hydriodici..... ʒ iii
 Aquæ..... ad. ʒ iv
 M. Sig.—4 cc. in water t. i. d. p. c.
 (Fla.)

CHAPTER V

ADJUSTED SOLUTIONS

COLLOIDAL SOLUTIONS, AMPULS, PARENTERAL SOLUTIONS, ISOTONIC SOLUTIONS

Colloidal Solutions. Solutions in which the body dissolved is in a colloidal condition; i.e. not ionized to any extent.

Ampuls (Lat. *Ampullæ*) Glass containers, usually hermetically sealed after filling, holding a single dose of a solution, or suspension, or powder, in a sterile condition, and intended for hypodermic or parenteral administration.

Isotonic Solutions. Solutions having the same osmotic pressure as the

fluids with which they are to be combined; i.e. usually the body fluids.

Hypodermic Solution. (Lat. *Solutio hypodermica*, or *Liquor hypodermicum*.) A clear sterile solution or a fine suspension intended for injection into or under the skin.

Parenteral Solutions. A general term which includes all solutions intended for hypodermic, subcutaneous, intramuscular or intravenous administration.

COLLOIDAL SOLUTIONS

About 1887 Arrhenius, one of the founders of physical chemistry, first published his theory of the dissociation of electrolytic salts in solution. The idea that a salt (sodium chloride, for instance) when dissolved in water became dissociated into electrolytically charged atoms or ions—sodium and chlorine—was so startling that it required some years for the chemists of the world to become accustomed to it.

But the theory has proved good, at least when properly qualified. Like all truths it has its limitations.

Colloidal solutions mark the other side, where the dissociation theory does not hold. The essential difference between a true solution and a colloidal solution may be stated as follows: In a true solution of an electrolyte we have dissociation, so that the salt is found in the atomic or ionic condition; while in a colloid solution the salt exists in the molecular condition, or in an aggregation of molecules. Thus a colloidal solution is, in a sense, a coarser form of solution. The proper term for it is a "dispersoid," the term "solution" isn't strictly right.

Like most natural phenomena there is no sharp line of demarcation between the two classes of solutions, but one merges into the other. We have grades of fineness, from true solution in which no particles can be seen by any optical means, to colloid solutions in which the particles can be seen by means of the ultramicroscope, and the still coarser suspensions in which the solid is seen to be suspended rather than dissolved.

Some bodies, such as gelatin, acacia, albumin, casein, etc., normally dissolve to give colloidal solutions. They are themselves called colloids. Other bodies, as sodium chloride, potassium sulphate, salt-

petre, and so on, form true solutions normally, but can be made to form colloidal solutions. Usually colloidal solutions are less stable and less transparent than true solutions, and the pharmacist is rarely if ever called upon to supply a colloidal solution when a true solution can be made. But often the solution which the pharmacist supplies in his dispensing is partially colloidal in character, and this is a strong reason for an understanding of such solutions on his part.

If we shake red mercuric oxide with an excess of distilled water we may find that the oxide will go into solution to the extent of 50 milligrams in a liter. If now we triturate some of the oxide in a mortar we note that as it becomes finer in powder it changes in color, finally becoming yellow; and then it may go into solution to the extent of 150 milligrams in a liter.

Powdering the oxide finely has resulted in making it three times as soluble, apparently.

But there is a difference in the character of the solutions. In the first instance the solution is clear and colorless; in the second it is clear if examined by transmitted light, but fluorescent and yellowish if examined by reflected light.

If now we evaporate the second solution to half its bulk on a steam bath we will find that red mercuric oxide has separated out and that the remaining solution contains only 50 milligrams of oxide to a liter. In other words, when the colloidal solution is disturbed it is the red oxide that separates out, and the remaining solution contains the oxide to the extent of the solubility of the red oxide.

This experiment illustrates the first principle in the making of colloid solutions, namely, *to reduce the substance to as fine a condition as possible*. Sand, for instance, is regarded as being quite insoluble in water, but if sand be ground fine enough it will dissolve to a considerable extent. The same is true of sulphur, silver, gold and other "insoluble" bodies.

Probably all "insoluble" bodies can be obtained "in solution" if ground to such a degree of fineness that the particles will display Brownian movement in water.

Brownian movement is the continuous motion exhibited by all solid bodies when reduced to an extremely fine condition and suspended in water or other liquid. The Brownian movement of extremely small particles offsets the attraction of gravity and the particles remain indefinitely in suspension. And they are so small that they do not interfere with the transmission of light, hence they cannot be seen and the solution is clear. But they will reflect light, and so the liquid is opalescent by reflected light. Thus, in fact, colloidal solutions are really suspensions of particles so very fine that they do not interfere with the transmission of light, but, rather, will reflect light. And by means of the ultramicroscope the reflected light from individual particles is clearly seen, thus proving their existence.

Colloid solutions therefore **mark the border-line** between true solutions and mechanical suspensions. In some cases the body in solution is so fine that it cannot be seen even with the ultramicroscope, and in other cases the particles are so large that the liquid appears cloudy but will not settle. In the latter case they are termed emulsoids or suspensoids.

Colloidal solutions diffuse very slowly, exert little or no osmotic pressure, and do not materially affect the freezing or boiling points of the liquid.

It may be inferred that since they resemble suspensions they must be less stable than true solutions. This is a fact. Anything that tends to coagulate the particles in a colloid solution will break the solution. When coagulation begins it is likely to separate out all of the colloidal matter. Many things will accomplish this.

Strong agitation continued for a time will sometimes cause separation. Thus a solution of pepsin or of albumin can be coagulated by continuous shaking.

The addition of an electrolytic salt or a current of electricity may coagulate the colloid. The particles in a colloid solution are usually all charged with the same polarity—either positive or negative. Particles thus charged are driven apart by the electrical force. But if to a positively charged solution a negatively charged body is added the attraction of the two different charges will overcome the repulsive force and coagulation will occur.

If a colloidal solution which is positively charged be mixed with another colloidal solution which is negatively charged, the mutual attraction of the charges will cause precipitation of both charges. Hence colloidal solutions may be upset by the addition of salts which form true solutions, or by mixing with certain other colloids. Some solutions are very sensitive in this regard and some are not. Thus a colloidal solution of gold is precipitated by the addition of just a trace of salt, while soap requires a considerable amount of salt to throw it out.

For this reason many of the colloidal solutions used in pharmaceutical dispensing are **protected solutions**. That is, they contain not only the particular compound which is intended but also some colloid-like gum, gelatin or albumin which has the same electrical charge and which is not easily precipitated. The more stable colloid protects and holds up the less stable one.

Many of the silver compounds used in medicine produce colloidal solutions. For instance, argyrol, protargol, collargol, nargol, silvol, neo-silvol, etc., are not merely compounds of silver with the proteins, but they contain a sufficient excess of the protein to stabilize the solution. In such cases a marked excess of the protein is needed. Sometimes a slight trace of gelatin will cause precipitation, whereas a larger amount will prevent it. Mercury, zinc and other heavy metals will form colloidal solutions with these protein bodies.

Iron salts are protected in a similar way by sugar. Saccharated oxide of iron makes a colloidal solution in which the sugar acts as a protecting colloid. Invert sugar is stated to be about seven times as effective as cane sugar in holding up ferric hydroxide. Glycerin acts similarly. This explains the importance in compounding of mixing iron solutions with syrup or glycerin before adding an alkali or other incompatible ingredient. Glucose acts more by absorption, but the results are essentially the same.

The pharmacist is rarely called upon to make a distinctly colloidal solution, though in the course of usual prescription compounding he may frequently make a partially colloidal mixture, as has been suggested.

The tendency in medicine is more strongly toward the use of colloidal remedies, and the pharmacist will be better prepared for compounding who has a definite idea of colloidal conditions and the methods of securing and holding them.

From the pharmaceutical standpoint the methods of making colloidal solutions (other than simple solutions of the natural colloids) may be grouped as electrical, chemical and mechanical methods. In all cases the primary object is first to get the solid into an extremely fine, almost molecular condition. The particles must be fine enough to display the Brownian movements, and no particle having a diameter larger than 4 microns will do this. The smaller the particles the more rapid will be the Brownian movements and the more stable the solution. And probably the Brownian movements explain the non-settling of the particles.

Electrical methods are valuable for experimental work, but are not now adapted to solutions designed to meet commercial conditions.

If a current of electricity be passed between two gold wires immersed in water so as to form an electric arc at the ends of the wires, the gold will be gradually disintegrated in a very fine condition and will go into solution. The water used must be very pure and the solution so made is very sensitive. The addition of a minute quantity of salt, violent agitation, heating or other factors may cause the gold to agglomerate and separate out.

Similar results may be obtained by passing an electric current through a dilute solution of gold chloride, so that the gold is reduced and thus will go into solution in metallic condition. This solution is also sensitive to slight disturbances. Colloidal solutions of a number of the metals have been prepared by these methods, but they must be carefully preserved or the metal will be precipitated.

Chemical methods are better adapted to commercial conditions. Any kind of a chemical reaction which produces a molecular or colloidal body may yield a colloidal solution. In many cases the presence of a colloid in solution aids greatly in producing a colloidal solution.

Colloidal silver solutions may be made by precipitating silver nitrate with sodium hydroxide in the presence of gelatin, casein, albumin or derivatives of albumin. Or by precipitating silver iodide or chloride in the presence of gelatin.

These are typical of the methods which are used for many of the commercial colloidal solutions and compounds. By suitable methods of purifying and drying these silver compounds are obtained in a dry form which is readily soluble in water.

Colloidal solutions of Prussian blue are obtained by precipitating it in the presence of a gelatin solution.

Barium sulphate solutions have been prepared by precipitating in the presence of acacia or of sodium citrate.

Copper hydroxide is rendered soluble by sugar and also by casein.

Calomel yields a colloidal solution in the presence of albumin.

Sodium citrate renders aluminum hydroxide and silver salts soluble, as well as barium sulphate and iron salts.

Sugar prevents precipitation of copper hydroxide, ferric hydroxide and silver chromate.

Sodium sulphide will produce colloidal solutions of some metallic sulphides when ammonium sulphide will not.

In making colloidal solutions of this character it is probable that the gelatin or other colloid acts in two ways. First it causes a finer precipitate to form and prevents coagulation. Since coagulation is promoted by vigorous agitation, this should be avoided when a colloidal solution is desired.

Second, the colloid body promotes solution by "**peptization**"—a term that doesn't explain much but is convenient to use. It comes from the "peptizing" action of pepsin upon coagulated egg albumin, whereby the latter is rendered soluble. So in making colloidal solutions, compounds which promote the solubility of other bodies, without entering into combination with them, are termed peptization bodies. Soluble citrates thus peptize iron compounds, showing that the peptizing body is not necessarily itself a colloid.

Many colloidal or semi-colloidal solutions are obtained through hydrolysis. If a dilute solution of ferric chloride be heated for a few minutes it darkens in color, changing from a straw color to a reddish brown, becomes opaque by reflected light, and it may no longer give a blue color with potassium ferrocyanide. The water has hydrolyzed the salt, producing a basic oxychloride. If to a strong solution of ferric chloride ammonia water be added cautiously until a slight precipitate is formed which will not redissolve on standing, then the liquid be filtered and then subjected to dialysis, a very basic oxychloride of iron will remain in solution and the solution will have markedly colloidal properties. This is the method of making dialyzed iron.

Another way of accomplishing the same result is the process of making Solution of Ferric Oxychloride, N.F. IV, in which the iron is first entirely precipitated as hydroxide, this is washed free from soluble salts, then a small amount of hydrochloric acid is added and the mixture warmed until all the hydroxide has dissolved.

Basic compounds of aluminum, zinc, chromium and other metals are obtained in similar ways. Or at times a simpler method of dissolving the oxide in a chloride of the same metal.

Reduction methods are used in making solutions of the metals, a salt of the metal being reduced by formaldehyde, hydrazine or other reducing agents. Even light may reduce metallic salts to form a colloidal solution.

Oxidation methods are rare, but a colloidal solution of sulphur has been made by oxidizing hydrogen sulphide.

Mechanical methods are coming more into use. Since colloidal solutions play an important part in the technical arts there has been sufficient incentive to develop mills which will grind the more friable bodies sufficiently fine so that they will form colloidal solutions with water. Such mills must start with powders, and the grinding operation is carried on in the presence of water or another fluid. But they are made to work fast enough so that the grinding is continuous, the material flowing out as it is being fed in.

Such mills are being used for the preparation of colloidal solutions of sulphur, copper, silver, graphite, inks, paints, polishes, lubricants, etc., also for the preparation of materials for chemical action, as fats

for making soap by a cold process, cellulose for fermentation, nickel for use as a catalyst, etc., or for making emulsions, plastic masses or materials where an extremely fine subdivision is needed. They again prove that the key to colloidal solution is to first obtain the substance to be dissolved in an extremely fine condition.

From a pharmaceutical standpoint the subject is of more direct interest in that it discloses means for avoiding or overcoming many incompatibilities in prescriptions.

All colloids or colloidal solutions are not necessarily amorphous. Some crystalline salts or compounds have markedly colloidal properties when in solution, and the solutions act as protective colloids. The citrates of sodium, potassium and ammonium are especially valuable in this way. They prevent precipitation of the hydroxides or carbonates of most metals, particularly of iron, manganese, copper, zinc, antimony, bismuth and mercuric salts, and act similarly on some of the insoluble phosphates, and calcium and magnesium salts. Thus the alkali citrates can prevent precipitation by alkalis in most liquids. Tartrates have the same properties, but not as markedly as citrates, while salicylates, succinates, and benzoates also show similar properties.

Glycerin, sugar solutions, honey, and gums are also often effective in preventing precipitation in prescription combinations.

Note that all of these are effective in preventing precipitation, but not for dissolving precipitates already formed. Their value therefore lies largely in the ability of the operator to foresee incompatibilities and to avoid them by the needed method of compounding, or a possible change in the solvents that are used.

Sometimes a true crystalloid aids in forming a colloidal solution. Solution of oxychloride of iron, or Dialysed Iron, and solution of oxysulphate of iron are instances. In these cases an insoluble iron salt is peptized by a very small proportion of the normal salt and a solution thus formed. In the case of solution of oxychloride of iron, ferric hydroxide is precipitated and washed free from soluble salts, then a small amount of hydrochloric acid is added which forms some ferric chloride and this ferric chloride dissolves or peptizes the ferric hydroxide and so forms a solution. The addition of some glycerin then aids in stabilizing the solution. If a more basic solution is desired, the liquid is subjected to dialysis and some of the ferric chloride is dialyzed out without precipitating the ferric hydroxide. It is thus found that one molecule of ferric chloride will peptize as many as twenty-two molecules of ferric hydroxide and form a fairly stable solution. That such a solution has a markedly colloidal character is shown by the cloudy appearance which it shows in reflected light, and by the fact that silver nitrate will not produce the usual precipitate of silver chloride unless the iron solution is previously heated with an excess of nitric acid.

Colloidal solutions may have water, alcohol, oil, or any other liquid as the solvent. For oil solutions, woolfat, cholesterol, lecithin or oleates may act as stabilizing agents. Such solutions apply in pharmacy to liniments, ointments or possibly sprays. Unguentum Crede, an ointment of colloidal silver is an instance. Colloidal liniments and ointments are rare, just as colloidal solutions in general are the exception, but some of the common external preparations,

such as liniment of soft soap, compound liniment of soft soap, ointments of lead oleate and of zinc stearate and the oleates are examples. These are solutions of a naturally colloidal agent in the base or solvent.

Since most of the solutions or liquids of the body are colloidal in character, it has been reasoned that colloidal solutions or bodies will have a more energetic or persistent action than the same substance in crystalloidal solution or form. There is some clinical reason for supporting this theory, and colloidal solutions of some of the metals, notably silver, gold, lead, copper, mercury, and bismuth are offered as special medicaments. Most of these belong to the class of protected colloidal solutions. Colloidal solutions of sulphur and of iodine, also of quinine and of cocaine and other alkaloids are also offered, and find some use.

The alkaloids, particularly quinine and cocaine are found to be more active when in alkaline colloidal solution. English pharmacy has long favored the official ammoniated tincture of quinine, in spite of its strongly bitter taste, as a means of securing the action of quinine. Doubtless there are good reasons for its continued use. This suggests that prescriptions in which quinine salts are directed to be combined with an alkali may not be cases of oversight or ignorance, but an attempt to present the quinine in a more active condition than in simple solution.

Cocaine and its derivatives or substitutes, such as eucaïne, procaine etc. is stated to be three or four times as active in alkaline or colloidal solution as in the common solution of its salts. The colloidal and alkaline solutions are, however, instable, though they are offered to some extent in the market. More recently combinations of cocaine (also its substitutes) with boric acid, known commercially as borocaine, has had similar claims made for it. It is stated that solutions of borocaine are stable, but that boric acid being a feeble electrolyte the salt does not ionize but simply hydrolyses into acid and base, and the base being chemically the stronger imparts a slight alkaline reaction to the solution and a more energetic physiological action results. Solutions of borocaine are more stable than colloidal solutions of cocaine, but are much less so than solutions of cocaine hydrochloride, and the former are stated to deposit cocaine on standing.

As a rule colloidal solutions reach the saturation point more quickly than do crystalloids, and are therefore not very concentrated. This is particularly true of those which are not protected by a natural colloid, or in which the protecting agent is itself sensitive. Even strong agitation may cause some colloidal solutions to coagulate. Heat spoils some, and the addition of salts, acids or other bodies is always somewhat risky. Even the mixing of two different colloidal solutions may result in mutual precipitation. This applies to true colloids, but most of the colloidal solutions of pharmacy are either semicolloidal or are protected solutions which are quite stable except when a direct chemical incompatibility is involved.

The theoretical basis for advocating colloidal solutions for medicinal use is that the medicinal agent being in a molecular or polymolecular form presents a relatively large surface for action, and may also exert a catalytic action, approaching to that of enzymes.

AMPULS

Ampuls are glass containers holding usually a single dose of a clear medicinal solution, or a fine suspension, intended for parenteral use, (hypodermic, subcutaneous, or intravenous injection) and preserving it in a sterile condition. They are usually small, holding one to ten cubic centimeters, but may have a capacity of a liter or more in special cases. Their shapes vary, as do bottles or other containers, but in most cases the neck is very small and the liquid is removed either by drawing it out into the syringe by suction or by breaking opposite ends and allowing the contents to drain out. Viscid solutions are usually dispensed in double-end ampuls so that the contents can be removed by drainage.

Ampuls are made of special quality glass, which is particularly resistant to the solvent action of water. Ordinary glass is sufficiently soluble in water to impart a sufficient alkaline reaction to precipitate



FIG. 3.—Forms of ampuls used for massive injections.

alkaloids or metallic salts, or even to cause decomposition of the medicament, when the solution is heated to sterilize. They should be tested by filling with distilled water containing one per cent of phenolphthalein test solution, then sealing and heating in steam or boiling water for six hours. If a pink color develops in the solution, or if the liquid within the ampul shows fine scales or chips floating in the liquid the glass is not suitable. The retail pharmacist will find it most satisfactory to purchase ampuls ready for use, but in emergencies they may be made from small test tubes by drawing out at a suitable distance from the bottom. Test tubes being made of resistant glass are better than ordinary glass tubing for the purpose. But the above test should be applied in all cases.

Solutions which are changed by action of light, such as apomorphine, physostigmine or ferric solutions, etc. are preferably dispensed in ampuls of amber glass. But protection may also be secured by dispensing in boxes.

Special care must be taken in selecting the solvents used in making ampul solutions. These solutions must not only be sterile when used, but must be free from irritating substances of all kinds.

Only freshly distilled water should be employed, for even distilled water provides growth for bacteria and a distilled water which has been kept for some days may contain enough bacteria to produce toxic

bodies when these are killed by sterilization. As one doctor put it, "the physician does not want to inject a bacterial graveyard into his patients." Thus the water used should have been distilled within two days and should be stored in perfectly clean vessels, and before making the solution the portion used should be sterilized by boiling for thirty minutes.

Oils which may be used as solvents must be entirely free from rancidity and must be as nearly neutral as possible. Most vegetable oils contain some free oleic acid, and if this is present to a marked extent it will cause irritation. Hence particular attention must be paid to the acidity and an oil selected which does not contain more than one per cent of free fatty acids.

In many cases the acidity of the solution itself needs adjusting to insure stability and reduce the irritating effects. Alkaloidal and mineral salt solutions need to be slightly acid to insure against precipitation or decomposition when heated in the glass, but since even small amounts of free acid are irritating to the blood fluids the



FIG. 4.—Various shapes of ampuls.

acidity must not be more than will insure stability. Herein is shown the necessity of selecting a resistant glass for the ampuls, which will not permit of slow changes in the solutions by its solvent action on the glass. In the case of colored solutions, such as the iron solutions, the acidity cannot be adjusted by means of indicators and special processes are necessary. This is a factor which limits the manufacture of ampul solutions on a small scale.

All solutions should be filtered, and the use of germ-proof filters is desirable. This sterilizes the solution as well as filters it. When paper is used it should not leave fibres in the filtered liquid. Germ-proof filters are often defective, and must be tested for bacterial leakage.

The filling of ampuls is an operation which calls for special methods. Since the necks of the smaller sizes are almost capillary tubes, they demand special apparatus for filling.

Two general methods are in use. For small operations the best is to fill from a burette or syringe provided with a fine outlet. For a burette, a hypodermic needle is attached by means of a short rubber tube, this needle is inserted into the neck of the ampul and the required amount of liquid is drawn in. Care should be taken to insert the needle well into the ampul and to avoid wetting the sides with the fluid since this often causes discoloration when the ampul is sealed. For viscous fluids, including most of the oil solutions, a veterinary syringe

with a graduated barrel is preferred. This allows of forcing the liquid into the ampul. For large-scale manufacturing filling machines are built on this principle, having a number of tubes graduated to hold the required amounts and operating by pistons or by compressed air.

The other is the vacuum method. The solution is placed in a suitable dish, the necks of the ampuls immersed in the solution and the whole placed in a vacuum apparatus. The air is then sucked out until only a small amount remains, then the pump is shut off and the air readmitted. The ampuls being partially evacuated the liquid is sucked up to take the place of the air, thereby filling the ampul. A partial vacuum only is employed so that the ampuls are not completely filled with solution, but only as a bottle is filled. The ampuls are then

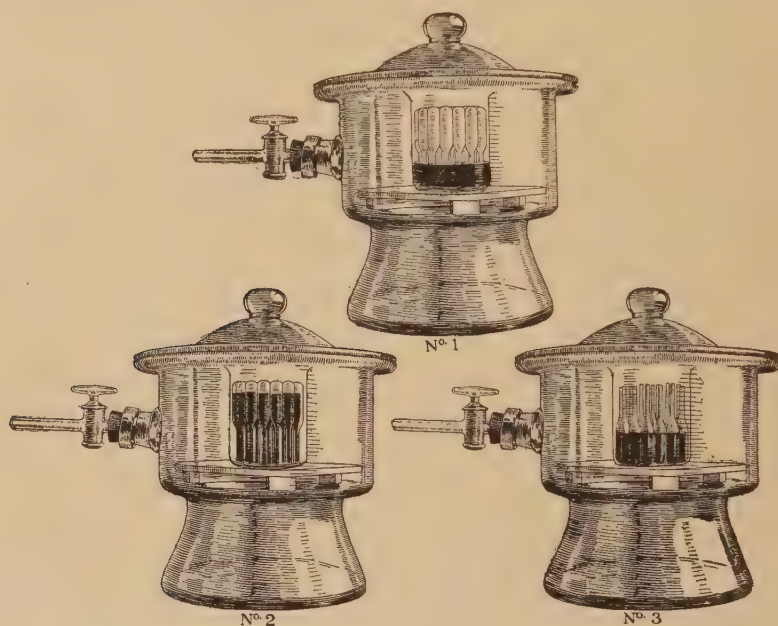


FIG. 5.—Filling ampoules by the vacuum process. No. 1 ampuls ready for filling; No. 2 ampuls filled; No. 3 ampuls ready for sealing.

reversed, necks up this time, and the vacuum reapplied. This sucks out the liquid which remains in the capillary necks and leaves them clear for sealing. But strong solutions, or those which char readily on heating must be washed to prevent blackening—which is one great objection to this process. This process also trusts to the regulation of the size of the ampuls and to the vacuum for measuring the amount of solution in each ampul, and it is very difficult to get them to fill evenly.

The ampul should contain slightly more than the dose which is to be administered. It is obviously impracticable to withdraw to the last drop, and moreover in making hypodermic injections it is customary to force out a drop or two of liquid from the syringe before inserting the needle to avoid forcing air into the tissues, and allowance must be made for these losses. Thus ampuls to supply 1 cc. doses should

contain not less than 1.1 cc.; for 2 cc. doses, 2.2 cc. etc. An excess of ten per cent is usually supplied on the smaller sizes.

Ampuls are sealed by holding the tip in the edge of a bunsen flame until the glass melts together. Care must be taken that the seal is complete. It is often of advantage to soften the tip in the flame, then close it by a touch of a glass rod, the tip of which is hot but not melted. The slight pressure closes the capillary point, and ensures a perfect seal.

If any of the solution remains in the tip it may char and blacken the tube, or even form a coating of carbonaceous material which later diffuses through the liquid, making it cloudy and unfit for administration. Some salt solutions will not blacken but will combine with the glass, making it soft or brittle and easily broken. These troubles are avoided by care in filling, or by washing the neck with distilled water after filling.



FIG. 6.—Filling and sealing ampuls.

Sterilization should be carried out promptly and thoroughly. When the ampuls are sterilized before filling, and the solvent before the solution is made the results are safer.

The ampuls are best sterilized by heating to 150°C . in an oven for an hour. Steam sterilization may be practised, but it is not as effective on spores.

Distilled water should be boiled for 15 minutes, then cooled, and the solution made in the flask in which the water was boiled.

When the ampuls are filled, they are best sterilized by immersing in boiling water or live steam for half an hour on each of three successive days. The spores which may be present and which are not killed at 100°C . will develop in the intervals and be killed in the next sterilization. Solutions which are sensitive to heat:—that is containing bodies which are injured or decomposed by a heat of 100 degrees, are pasteurized by heating to 60°C . for half an hour on three successive days. As an added precaution it may be advisable to add an

antiseptic, which increases the germicidal power of the heat, and itself is fatal to germs on long contact. For such purposes tricresol, phenol, chloretone etc. are preferred. The use of such antiseptics is also advisable for alkaline solutions, or for emergency cases where the standard three-day method cannot be followed. It makes an additional assurance of sterility.

Manufacturers of ampuls test each lot for sterility before placing them upon the market.

For extemporaneous preparation, when time does not permit of the three-day sterilization, some antiseptic is usually advisable. Sterilization by heat should not be omitted, but here the antiseptic aids because such agents are more active at higher temperatures and the single sterilization is more nearly complete when the antiseptic is present.

The addition of 0.5 per cent of phenol—which is favored in some hospitals, or of 0.3 per cent of cresol, is the plan usually preferred. Thymol (1 grain in 4 ounces) is sometimes used but thymol is not soluble enough for the best effects. In solutions of alkaloids the antiseptic aids in preventing fungus growths as well as bacteria.

The solvents employed in making hypodermic solutions are mostly sterilized distilled water, physiological salt solution, and vegetable or animal oils. Alcohol is too irritant for injection into the tissues, through it is occasionally used in small proportion preferably not exceeding 20 per cent of the total volume. Glycerin is also irritant for this purpose, and is avoided.

Vegetable or animal oils are used for medicaments which are soluble in these and are insoluble in water, or for suspending insoluble salts which are intended for slow absorption. Bodies like camphor, guaiacol, iodoform, eucalyptol, etc. are dissolved in a vegetable oil,—usually a neutral olive oil—when intended for hypodermic use. The oil must be as nearly free from acid as is practicable, and should be selected for this purpose. All natural oils will contain some free fatty acid, but the best grades will contain less than half of one per cent. If more than one per cent is present the oil is not suitable. It should also be sterile: heating to 120° C. for one hour will sterilize.

Insoluble compounds, such as subsalicylate of mercury, bismuth salicylate, mercury, etc. are suspended in a vegetable oil or in a semi-solid animal oil, such as goose grease. The oil is a better suspending agent than water, and it also hinders absorption, thus aiding in a slow and continuous action, which is desired. Mineral oil (liquid petrolatum) should not be used because it is not absorbed. Even the vegetable and animal oils are absorbed very slowly—from three to six weeks time being required before it disappears entirely from the site of injection.

Mercuric iodide, which is soluble in an aqueous solution of potassium iodide, is sometimes preferred in oil solution because it is very slowly absorbed in this form. It is only slightly soluble in oil, but its solution is aided by potassium iodide. G. E. Ewe found that cotton seed and castor oils are better solvents for it than almond, olive or sesame oils. It will dissolve to the extent of 4 milligrams per cc. or 0.4 per cent in oil. The oil should be warmed to aid solution, and if these proportions are not exceeded the mercuric iodide will remain

in solution on cooling. If olive oil is used the mercuric iodide should be triturated with one-third its weight of potassium iodide in a dry mortar, and the mixture dissolved in warm olive oil. Any excess of potassium iodide which does not dissolve must be filtered out.

HYDROGEN ION CONCENTRATION

When an immediate action of a medicine is desired, or when it is desired to have a medicine act at once upon the blood, it may be injected directly into the body tissues or the blood stream. Medicines so employed must be in perfect solution or in fine suspension in oil, if insoluble in water, since they are introduced through the skin by means of a hollow needle and enter immediately into the circulation.

When the solution is injected just under the skin, it is termed a *subcutaneous* or *hypodermic* injection; when it is injected into the deeper tissues it is properly an *intramuscular* injection though it may also be called a hypodermic; and when it is injected directly into the blood stream through the walls of a vein, it is an *intravenous* injection. The general term that includes all of these forms is *parenteral administration*.

The preparation of solutions for these purposes calls for extreme care and a high degree of skill. The solutions must not only be perfectly clear, but they must be sterile and free from irritating substances. Solvents like alcohol, glycerin and acids, which may irritate, must be avoided, or used in very small and carefully regulated amounts.

When it is considered that the fluids of the body are maintained within very narrow limits of acidity or alkalinity and also in definite solution strength, and that any material deviation from these limits will result in pain and shock or even death, it is plain that especial care is needed in the adjustment of solutions or the results may be highly detrimental rather than beneficial. Any abrupt change in the composition or reaction of the blood will produce a condition of shock in the patient which is dangerous and may be fatal. When small amounts of liquid are injected, the irritation may be local—at or close to the site of the injection—and the danger may be small though considerable pain may follow. When large amounts are injected there is real danger if they are not properly adjusted.

The two main factors to consider in the adjustment of these solutions are acidity and concentration.

Reaction.—The blood is very slightly alkaline, and is kept so by a very delicate mechanism acting through the lungs and the kidneys which neutralizes any excess of acid or alkali which may be introduced into the body through the mouth. It is also kept in a state of constant solution strength by the process of osmosis through the cells or tissues of the body. Thus while there is a constant introduction of new substances into the blood by the assimilation of food, there is a corresponding continual adjustment of the concentration and alkalinity in the life processes. When foods or medicines are taken in the natural way by route of the mouth, nature takes care of the necessary adjustments within the body. But when liquids are injected directly into the blood, it is necessary to adjust these to a reaction and concentration that will not be far from the natural conditions. For when fluids that have a

higher or lower acidity or alkalinity are introduced into the blood at a rate or in amount that the blood cannot neutralize, reactions characterized by chills and prostration follow.

This is the condition which the pharmacist must avoid in preparing solutions for parenteral injection, and it is frequently difficult to secure a satisfactory balance between the chemical character of the injection and the needs of the blood in maintaining a neutrality and concentration within its narrow limits. For most medicinal bodies which are injected into the blood need to be slightly acid for complete solution, and the solutions should be neither too concentrated nor too dilute or they may produce pain from too active osmosis.

Let us consider first the adjustment of the reaction of these solutions.

We know that the blood is slightly alkaline and it would seem like a simple proposition to make the solution to be injected correspondingly alkaline. But as before said, many of the medicinal agents which are used in this manner,—alkaloids for instance,—require a slightly acid medium for solution and the preservation of their activity. Hence many of these solutions *must* be acid. And we find further that the amount of acid present is not the whole question. The kind of acid used and the character of the other components of the solution make a marked difference.

This is because of varying degrees of electrolytic dissociation that different acids and salts display in solution. For instance hydrochloric acid (and most inorganic acids similarly) dissociates almost completely in dilute solutions into hydrogen ions and chlorine ions, the former carrying a positive electrical charge and the latter a corresponding negative charge.

This is characteristic of all electrolytes,—acids, alkalis and salts,—which conduct an electric current in a solution. The current is transmitted by the moving ions. Sodium chloride, in dilute solution, dissociates into Na and Cl, sodium sulphate into Na and SO₄, sulphuric acid into H and SO₄, nitric acid into H and NO₃, etc. These dissociated parts are termed ions, and in uniting with other bodies they react, not as whole acids or salts, but as ions. Thus hydrochloric acid, dissociated into H and Cl, reacts with sodium hydroxide, dissociated into Na and OH, by the H ion uniting with the OH to form HOH or water, while the Na ion unites with the Cl ion to form NaCl or sodium chloride.

But many chemical bodies are not electrolytes and do not thus dissociate. Sugar, for instance, dissolves perfectly in water, but it exists in solution simply as sugar. And it does not react actively with other chemical bodies. Also there are many chemical bodies which are feeble electrolytes and dissociate when in solution only to a very limited extent. Most of the organic acids are of this type. Acetic acid, for instance, dissociates only slightly into H ions and C₂H₃O₂ ions, or sodium acetate into Na and C₂H₃O₂. The first having a positive electric charge is called the cation, the latter having a negative electrical charge is termed the anion: but both are "ions."

Now since reactions take place between ions it follows that an acid which ionizes freely in solution will react with other bodies more vigorously than will an acid which ionizes feebly. The first may be termed

a "strong" acid and the second a "weak" acid. The first reacts energetically as an acid, the second weakly.

So we distinguish now between the *amount* of an acid present in a solution and its *activity* or *strength*;—between its combining energy and its neutralizing power. A normal (volumetric) solution of hydrochloric acid, for instance, is exactly equal to a normal solution of acetic acid in neutralizing power, but the hydrochloric acid in this strength is about 95 per cent ionized while the acetic acid is about 5 per cent ionized. Or to state it in another way, a normal solution of hydrochloric acid will contain 36.47 Gm. of HCl in a liter of which 1.008 Gm. is hydrogen, and 95 per cent of this, or 0.9576 Gm. is ionized hydrogen. And a normal solution of acetic acid will contain 60.03 Gm. of $\text{HC}_2\text{H}_3\text{O}_2$ in a liter, of which 1.008 Gm. is replaceable hydrogen, and only about 0.0504 Gm. is ionized hydrogen. So *in energy of action* a normal solution of hydrochloric acid is nearly twenty times as strong as a normal solution of acetic acid, though both have the same neutralizing power.

Similarly alkali salts are ionized in solution and liberate alkali ions.

Sodium hydroxide ionizes into Na and OH, sodium carbonate into Na and CO_3 , etc., but the hydroxide ionizes more freely than the carbonate hence the hydroxide is the more active or "stronger" alkali.

Now the degree or amount of ionization in an acid or alkaline solution of a specific strength is termed the *hydrogen-ion concentration*. This is dependent first upon the character of the acid or alkali in solution, and second upon the strength of the solution. In a dilute solution the acid or alkali is more highly ionized than in a strong solution. Temperature is also a factor in the case.

A normal solution in terms of hydrogen-ions will contain 1.008 Gm. of free hydrogen ions per liter, or if alkaline 17.01 Gm. of free hydroxyl (OH) ions per liter. And since these are the active ions in reactions they are both considered under the general term of hydrogen ions, and the symbol used for designating them is pH, standing for "potential hydrogen." This symbol pH then stands for *the amount of acidity or alkalinity which is directly active*.

Water, which for this purpose is best symbolized as HOH is but very slightly ionized. It is calculated that a liter of pure water will contain a large number of free hydrogen ions and a corresponding number free hydroxyl ions. These offset each other and would correspond to a ten-millionth-normal acid or alkali, or 10 raised to the minus 7th power (1 with 7 ciphers) so the neutrality of water is represented as pH7. In a solution which contains more hydrogen ions than hydroxyl ions the pH value is less than 7 and if more hydroxyl than hydrogen ions the value is more than 7. In practical work this symbol is not used for solutions more strongly acid or alkaline than a normal solution of the ions. This may be stated a little more plainly as follows:

A normal acid, fully ionized	= pH0 or 1 in	1 liters
A tenth-normal acid, fully ionized	= pH1 or 1 in	10 liters
A hundredth-normal acid, fully ionized	= pH2 or 1 in	100 liters
A thousandth-normal acid, fully ionized	= pH3 or 1 in	1,000 liters
A ten-thousandth-normal acid, fully ionized	= pH4 or 1 in	10,000 liters

A hundred-thousandth-normal acid, fully ionized	= pH ₅ or 1 in	100,000 liters
A millionth-normal acid, fully ionized	= pH ₆ or 1 in	1,000,000 liters
A ten-millionth normal acid, fully ionized	= pH ₇ or 1 in	10,000,000 liters
A ten-millionth-normal alkali, fully ionized	= pH ₇ or 1 in	10,000,000 liters
A millionth-normal alkali, fully ionized	= pH ₈ or 1 in	1,000,000 liters
A hundred-thousandth-normal alkali, fully ionized	= pH ₉ or 1 in	100,000 liters
A ten-thousandth-normal alkali, fully ionized	= pH ₁₀ or 1 in	10,000 liters
A milli-normal alkali, fully ionized	= pH ₁₁ or 1 in	1,000 liters
A centinormal alkali, fully ionized	= pH ₁₂ or 1 in	100 liters
A decinormal alkali, fully iodized	= pH ₁₃ or 1 in	10 liters
A normal alkali, fully ionized	= pH ₁₄ or 1 in	1 liters

Note that the above refers to *fully ionized* acids and alkalis,—not to the usual normal, decinormal, etc., solutions. Also that no normal solution is fully ionized, hence it cannot be of pH₀ or pH₁₄ value. The value of pH must therefore be found in some different way than by titrating the solution.

Two methods are in use for determining the hydrogen-ion concentration of a solution,—or in other words the pH value.

The most accurate method is by means of a *potentiometer*, which is an apparatus for measuring the difference in electric potential between the free hydrogen-ions and the solution under test, from which the pH can be calculated. This method requires an expensive apparatus and some skill in its use.

The other method is by use of indicators. It has been found that indicators which are used in volumetric titrations change their color within definite limits of acidity or alkalinity, and by finding the indicator that is most sensitive to the solution under test a fairly close estimate of the pH value can be ascertained. This method is limited to solutions having little or no color of their own which would obscure the color changes of the indicator. A series of indicators is needed, each being useful within its own limits.

The following shows such a series with the color changes:

INDICATOR	COLOR CHANGE	pH VALUE	INDICATIONS
Methyl Violet.....	Green to Blue	0.1 to 3.2	very acid
Thymol Blue.....	Red to Yellow	1.2 to 2.8	very acid
Brom-phenol Blue....	Yellow to Blue	2.8 to 4.6	quite acid
Toepfer's Reagent....	Red to Yellow	2.9 to 4.2	quite acid
Methyl Orange.....	Pink-orange-yellow	3.1 to 4.4	quite acid
Congo Red.....	Blue to Red	3.0 to 4.5	quite acid
Brom-cresol Green....	Green-yellow to Blue Green	3.8 to 5.4	quite acid
Methyl Red.....	Red-orange-yellow	4.2 to 6.3	slightly acid
Lacmoid.....	Pink-violet-blue	4.0 to 6.0	slightly acid
Azolitmin.....	Red to Blue	4.5 to 8.3	acid-neutral-alkal.
Brom-cresol Purple...	Yellow to Purple	5.2 to 6.8	very slightly acid
Brom-thymol Blue....	Yellow to Blue	6.8 to 7.6	acid-neutral-alk.
Phenol Red.....	Yellow to Red	6.8 to 8.4	acid-neutral-alk.
Cresol Red.....	Yellow-orange-purple	7.1 to 9.0	slightly alkaline
Meta-cresol Purple...	Yellow to Purple	7.4 to 9.0	alkaline
Thymol Blue.....	Yellow-green-blue	8.0 to 9.6	slightly alkaline
Phenolphthalein....	Colorless to Pink	8.3 to 10.0	alkaline
O Cresolphthalein...	Yellow to Purple	8.2 to 9.8	alkaline
O Naphtholphthalein	Red-green-blue	7.9 to 9.0	alkaline
Thymolphthalein....	Colorless to Blue	8.3 to 10.5	alkaline
Thymol Violet.....	Yellow to Violet	9.3 to 13.0	very alkaline

These indicators all change color gradually within the limits stated, and the best way to use them is to compare the color with a colored chart which is published for the purpose, or with solutions of known pH value.

Thymol blue, for instance, is red in acids stronger than a pH of 1.2 and becomes yellow at 2.8, then it very gradually acquires a blue tint as the solution becomes alkaline and at 8.0 it gives a yellowish green which becomes more and more blue until at 9.6 it is a pure blue, and no further change occurs. This indicator is therefore used at both ends of the scale but is of little value near to the neutral point.

For estimating the pH value by means of indicators the ten in *italics* are most useful. Then two or three may be needed to ascertain the approximate pH value of a given solution. For instance, suppose that we have a solution of pH value 6.4. The indicators tried in order will show as follows: Thymol blue, yellow; Brom-phenol blue, blue; Methyl red, yellow; Brom-cresol purple, purple. The solution therefore comes somewhere within the range of 6.0 and 6.8 because it is alkaline to methyl red whose limit is 6.0 and it is near to alkaline with brom-cresol purple. But with Phenol red it will be yellow, indicating acid. It is therefore between 6.0 and 6.8. With a color chart or with known solutions to compare by the exact value can be ascertained by comparing the color obtained with Brom-cresol purple. Otherwise we shall have to be satisfied with the finding that it is somewhere between 6.0 and 6.8—which is near enough for many purposes. As a means of saving time a mixture of the indicators methyl red, naphtholphthalein, phenolphthalein, thymolphthalein and cresolphthalein (also known as cresol red) has been proposed. This is stated to give a pale red color at pH₃, red at pH₄, orange-red at pH₅, orange at pH₆, yellow at pH_{6.5}, greenish yellow at pH₇, green at pH₈, blue at pH_{9.5}, violet at pH₁₀ and reddish violet at pH₁₁. Some practise, and preferably comparison with a standard color chart is necessary to estimate the values in this way.

It might be inferred that the pH value of a solution could be regulated by titration after selecting the proper indicator. In a pure solution of a strong electrolyte, like hydrochloric acid, or in a pure solution of an acid or alkali whose dissociation constant is known, close results might be obtained by this method. But in none except extremely dilute solutions do we have complete dissociation. In most acid solutions we have a mixture of dissociated hydrogen ions, dissociated acid anions and undissociated acid, and it is the dissociated hydrogen ions only that we are now seeking. Moreover in titration we dilute the solution and so change the dissociation. Titration of an acid with an alkali gives us the total amount of acid present, both dissociated and undissociated; it does not measure the hydrogen-ion concentration.

Furthermore salts of weak acids may be present which interfere with the dissociation of the acid or alkali. These are called *buffers*. Their presence in a solution reduces dissociation and thus reduces the hydrogen-ion concentration.

¹ For a method of accurately determining the pH value of any colorless solution by means of indicators, see articles by L. J. Gillespie in *Journal American Chemical Society*, 1920, page 742, and by W. D. Hatfield, *J. Am. Chem. Soc.*, 1923, page 940.

In the human body the two salts which act mainly as buffers are sodium bicarbonate and sodium phosphate.

Sodium bicarbonate dissociates in water into Na and HCO_3 and the latter reacts with water to form H_2CO_3 and OH. The first (H_2CO_3) is an acid which dissociates but slightly and is therefore a weak acid, and the OH is alkaline which offsets the acid. The solution is therefore neutral unless some carbonic acid be lost through agitation or heat, when it will be alkaline. Now if we add an acid to the solution of bicarbonate we have a reaction like the following:



And since H_2CO_3 is a weak acid we have very few hydrogen ions present until after all of the sodium bicarbonate is decomposed. So conversely the presence of sodium bicarbonate in a solution will permit of the addition of enough acid to entirely decompose it without changing the pH value very much.

Sodium phosphate may exist as an acid salt— NaH_2PO_4 or as a basic salt Na_2HPO_4 . If we add acid to the latter we may change it from Na_2HPO_4 to NaH_2PO_4 —but both the anions HPO_4 and H_2PO_4 are very weak which dissociate very slightly, so the pH value of the solution is not changed. Thus we can add to a solution of sodium phosphate enough acid to entirely change its composition without materially changing the hydrogen-ion concentration, because the weak acid liberated by reaction does not dissociate sufficiently. Likewise we can add an alkali to NaH_2PO_4 and we merely change it to Na_2HPO_4 which has about the same dissociation value, and so the alkali does not appear in pH values. Now in either case the acid or the alkali are present, and can neutralize other alkalis or acids, but they do not show in hydrogen-ion concentration. Or if we add hydrochloric acid to a solution of sodium acetate we have the reaction $\text{NaC}_2\text{H}_3\text{O}_2 + \text{HCl} = \text{NaCl} + \text{HC}_2\text{H}_3\text{O}_2$ and since acetic acid dissociates far less than hydrochloric the hydrogen ions freed will be far below the proportion of hydrochloric acid added.

It is the two buffer salts, sodium bicarbonate and sodium phosphate, which occur in blood and tissue fluids and maintain the reaction of the body fluids. They give time for the fluids to absorb the products of metabolism and to neutralize the excess of acid. Then the acid is eliminated from the lungs as carbonic acid, or from the kidneys as phosphates. Thus the normal reaction of the tissues is maintained.

Buffer salts then act by changing free acting acids or alkalis into relatively inactive acids or alkalis. In the body they convert the acid energy into acid inactivity and provide for the elimination of the excess. This explains the importance of distinguishing between total acid and free hydrogen ions in solutions for injection.

Buffer salts include all weak electrolytes, such as the salts of organic acids, phosphates, borates, carbonates, etc., and also the non-electrolytic organic compounds like sugar, proteins, albumins, peptones, gums, etc.

Note that buffers do not neutralize the acids or alkalis. They simply change them into the less active forms so that they do not exert the same energy in reaction. They restrain the action of the acids or alkalis on other substances.

The body fluids are all buffered by the salts, proteids and sugars present, so that the introduction of any extra acid or alkali into them will be retarded in action. The pH value of some of these fluids is as follows:

Gastric juice (adult).....	0.9 to 1.8	(acid)
Perspiration about.....	5.0	(acid)
Saliva.....	6.9	(slightly acid)
Tears.....	7.2	(faintly alkaline)
Blood.....	7.4	(faintly alkaline)
Pancreatic juice.....	8.4	(alkaline)

The digestive juices may be very acid or markedly alkaline, and they vary according to food and digestive conditions. Perspiration also varies somewhat with conditions, but the blood is held to very close reactions.

In preparing solutions for injection into the blood stream it is desirable to have the solution as near in reaction to that of the blood as possible. But it is seldom possible to secure this because the chemical properties of the medicinal agents which are used in this way more often demand an acid solvent—sometimes a very markedly acid solvent.

When an acid solution is injected in very small quantities,—or when it is injected very slowly (which is required in intravenous injections) the blood can buffer and so take care of quite an amount of free acid. But the solution so injected should not contain much acid together with buffer salts or bodies, for the buffers in the solution and in the blood may not act well together and the acid must be taken care of whether it is buffered or not. In fact it has been learned that the blood can take care of an unbuffered acid solution much more easily and quickly than of the same amount of acid when it is buffered. In experiments on frogs it has been found that when an unbuffered solution is injected it may have a pH range of 2.9 to 9.35 without causing reactions; if weakly buffered it can vary only from 4.2 to 7.45, and if strongly buffered it must be within the range of 5.65 to 6.6 to avoid reactions. This indicates that the less an injection fluid is buffered the more readily it can be adjusted by the tissues to a reaction approximating that of the blood.

Therefore in preparing acid solution for injection the pH value should not be reduced by adding buffers. If a considerable amount of acid is necessary it is better taken care of by slow injection or by considerable dilution than by buffering.

The essential point to consider here is that when a simple acid or alkaline solution is injected the irritation which may be caused is proportionate to the dissociation of the acid or alkali. Hence organic acids and carbonated alkalis are more easily adjusted than mineral acids or caustic alkalis. The difference is indicated by the hydrogen-ion concentration.

But when buffered solutions are injected the total quantity of acid or alkali present must be considered, because the system must neutralize all of the acid or alkali before it can be properly absorbed.

Care is also in selecting the distilled water. Strange though it may seem the preparation and preservation of a strictly neutral

distilled water is not easy. Furthermore on storing, a distilled water tends to become acid, often markedly so, through absorption of CO_2 and when used as a solvent it may produce a solution with a much higher pH acidity than that of the blood. Boiling, for sterilizing may also develop acidity, and if the solution contains glucose it will certainly do so.

For eye washes or mouth washes the situation is different, and it may be advisable to buffer these solutions, since the solution does not circulate through the system but is used locally. A buffered and isotonic solution may then be made by dissolving 0.81 Gm. of pure sodium chloride, 0.96 Gm. of pure sodium phosphate, and 0.18 Gm. of pure potassium phosphate in a liter of neutral distilled water.

Buffering phosphate solutions are made by dissolving 11.876 Gm. of U. S. P. sodium phosphate in a liter of neutral distilled water, and 9.078 Gm. of pure potassium phosphate in a liter of neutral distilled water. These solutions are mixed in the proportion of 4 parts of the sodium solution to 1 part of the potassium, and when used physiologically 1 part of the mixed solutions is mixed with 9 parts of physiological salt solution.

Solutions of alkaloids,—morphine, atropine, cocaine, hyoscyamine, etc., and of some other active bodies like strophanthin, adrenalin, pituitrin, etc., are not stable in even faintly alkaline solutions, and if strictly neutral will dissolve enough alkali from the glass in which they are sterilized or stored to partly decompose or precipitate them. Such solutions must be made slightly acid, but should be as near to the neutral point as conditions will permit. When practicable an organic acid is to be preferred to an inorganic acid because the former does not dissociate as much in solution.

Alkaloids, gland principles or other bodies which require an acid to get them into solution, must of course contain the needed acid in the solution. In selecting the acid for these the chemical peculiarities of the body must be considered. Thus organic acids are not commonly suitable for quinine in solutions which are to be sterilized by heat or are to be stored for any length of time, because the organic acid causes the quinine to polymerize and form quinotoxin (or quinicine) which is toxic. The chemical requirements of the active constituents must be considered first.

Alkaline solutions should not contain free caustic alkali when a carbonate or bicarbonate will serve the purpose. If caustic alkali is necessary it must be employed cautiously. Solutions intended for intravenous use are usually more dilute and of larger bulk than solutions used hypodermically. And all solutions used for injection or for collyria should be as nearly as possible isotonic as well as near to neutral.

The ampuls of the National Formulary V will give some idea of the adjustment of acid or alkali that is necessary in solutions of various types. These are among the simpler problems in this line, and manufacturers usually draw the lines closer than in the formulas that are there given. No line of pharmaceuticals calls for more care in their preparation than that of ampuls, and special equipment as well as practise is required for their preparation.

The application of hydrogen-ion concentration to prescription mixtures will be rarely necessary, yet it may come into play occasionally. The following prescription shows how it may apply.

R. Liq. Potass Citratis.....	3 iv
Caffeinae Citratis	
Methenaminae	
Potassii Acetatis	aa 3 ii
Aq. Menth Pip.....	3 ii
Pt Sol.	

Sig.—A teaspoonful every 3 hours.

This prescription contains four very soluble salts, and by dissolving the citrated caffeine in the peppermint water and adding to the solution of the others in the solution of potassium citrate a clear liquid is easily obtained. But after standing a short time caffeine crystallizes out in a mass of crystals that quite prevents the dispensing of an even dose.

This is explained as follows: The citrated caffeine is a mixture of equal weights of caffeine and citric acid, the function of the latter being to render the caffeine more soluble in water. This it does in the above mixture until the buffer action of potassium citrate and potassium acetate comes into play and reduces the activity of the acid. The caffeine then behaves as if no acid were present, and is salted out by the other ingredients.

This is shown in the fact that if the citric acid be doubled less of the caffeine crystallizes out, and if it be quadrupled still less crystallizes. Furthermore if hydrochloric acid be used in molecular proportions in place of citric a further reduction in the amount of crystals separating will ensue. The crystallization can therefore be prevented by adding acid, but this will decompose the methenamine, which is not intended. One should not dispense formaldehyde, even as a decomposition product, when methenamine is intended. The only proper procedure in this case is to add water to make a 12 ounce solution instead of a 6 ounce, and, of course, double the dose. The physician who wrote the prescription should be consulted.

ISOTONY AND ISOTONIC SOLUTIONS

Since all of the fluids and secretions of the body contain dissolved substances, in quite definite proportions, these fluids will exert a certain definite osmotic pressure which is uniform for each fluid. If another solution is introduced into the circulation, or applied to the eyes, it may have less or more of substance in solution or the dissolved substances may be of a different character than those of the natural body fluids, hence it will have a different osmotic pressure. When a liquid has a lower osmotic pressure than the body fluid with which it is mixed it is **hypotonic**; when it has a higher pressure it is **hypertonic**; and when it has the same pressure it is **isotonic**.

Whether any given solution is isotonic depends upon (1) the amount or proportion of dissolved substances which it contains and (2) upon the character of those substances. Salts which dissociate freely in solution exert a greater osmotic pressure than those which dissociate slightly or than organic non-dissociating bodies. So the type

of the dissolved substances is of more importance, from the osmotic pressure standpoint, than the amount in solution.

The practical value of this subject lies in the fact that hypotonic or hypertonic liquids when applied to the eyes, or when injected into the circulation in considerable amount, may cause pain because the difference is osmotic pressure between the solution and that of the natural body fluids is felt in pressure upon the tissue cells during the time of establishing an equilibrium. This may be easily illustrated by putting a few drops of distilled water (not ordinary tap water) into one eye and a drop or two of a concentrated solution of sodium chloride into the other eye. In both cases the eye will smart for a few moments because in one case the distilled water draws the salts from inside of the eye until the water contains an equal amount, and in the other case the excess of salt is absorbed through the membranes. When a small amount of liquid is injected into the blood stream it is quickly diluted so that the osmotic difference is not felt. This adjustment of osmotic pressure is therefore commonly of more importance in collyria than in hypodermic solutions, particularly with children, who resent and even fight painful or unpleasant measures.

First, a brief consideration of **the principles involved**. Blood serum is composed of about 8.8 Gm. of inorganic salts, largely sodium chloride, and about 83 Gm. of organic matter, chiefly colloidal in character, per liter. It freezes at -0.55 to -0.56° C. The lachrymal secretion is thinner and contains less colloidal organic matter, but more salt. It freezes at about -0.80° C. corresponding to 1.4 Gm. of sodium chloride per liter. Now since tonicity refers to the tension of the tissues, and that is a matter, in this case, of osmotic pressure, it is plain that a solution which contains less than 8 Gm. of sodium chloride in 1000 cc. will, if injected under the skin, cause osmosis of salt from the serum and if the difference is great enough it will cause pain until an equilibrium is reached. (Since the composition of blood serum will vary slightly the standards of salt strength are considered as 7.5 to 9.5 Gm. of sodium chloride per 1000 cc.) And since the lachrymal (tear) secretion is stronger in salt than blood serum, a collyrium should contain close to 1.4 Gm. of sodium chloride, or its osmotic equivalent, in 1000 cc. to avoid temporary smarting.

The osmotic pressure comes from the diffusion of the inorganic salts, the organic colloidal substances only acting as hindrances to rapid diffusion. So the main emphasis in isotony is placed upon the salt content, though similar results can be obtained by adding colloidal bodies.

This is all aside from the special action of the medicinal substance. An irritant will be irritating even if isotonic. Also the acidity of the solution is a factor. But very slight amounts of acid or of alkali (not caustic) are not irritating in themselves. Yet solutions for this purpose should be made as nearly neutral as is consistent with stability and activity. It is well also to bear in mind that slightly acid solutions are better borne if a little hypotonic (weak), while alkaline solutions are better if slightly hypertonic (strong). Most alkaloidal solutions for injection, or for sterilization, must be made slightly acid to prevent decomposition.

Whether a solution is isotonic—*i. e.*, has the same effect or tonicity upon the tissues of the body—therefore depends (1) upon the amount

or proportion of dissolved substance which it contains, and (2) upon the character of those substances. Both of these are shown by the freezing point of the solution, for all substances in solution lower the freezing point in proportion to the amount present, but in different degree. The greater the dissociation of the salt, the more it affects the freezing point.

Formulas have been offered by which the amount of any salt needed to produce an isotonic solution can be calculated from the freezing point. But these formulas have not proved entirely satisfactory.

Lumiere and Chevrotiere (*Bull. sci. pharmacol.*, through *Chem. Abst.*, 1914, 2106) have given the following list of freezing points of weak solutions which are convenient for use in collyria and hypodermic solutions.

1.7 per cent Boric acid.....	-0.56°	C.
0.5 per cent Alum.....	-0.05°	C.
1.0 per cent Alum.....	-0.10°	C.
0.3 per cent Formaldehyde.....	-0.15°	C.
1.0 per cent Formaldehyde.....	-0.30°	C.
10.0 per cent Protargol.....	-0.18°	C.
1.0 per cent Borax.....	-0.22°	C.
1.0 per cent Cocaine Hydrochloride.....	-0.12°	C.
3.0 per cent Cocaine Hydrochloride.....	-0.35°	C.
1.0 per cent Atropine Sulphate.....	-0.075°	C.
3.0 per cent Atropine Sulphate.....	-0.25°	C.
1.0 per cent Morphine Hydrochloride.....	-0.099°	C.
0.9 per cent Sodium Chloride.....	-0.56°	C.
1.0 per cent Sodium Chloride.....	-0.58°	C.
1.4 per cent Sodium Chloride.....	-0.80°	C.
1.0 per cent Sodium Nitrate.....	-0.40°	C.
1.4 per cent Sodium Nitrate.....	-0.56°	C.
2.0 per cent Sodium Nitrate.....	-0.80°	C.
1.0 per cent Sodium Bicarbonate.....	-0.40°	C.
1.4 per cent Sodium Bicarbonate.....	-0.56°	C.
2.0 per cent Sodium Bicarbonate.....	-0.80°	C.
Tear secretions.....	-0.80°	C.

Solutions of silver nitrate and of potassium permanganate 1 in 1000 are too weak to show any freezing-point depression.

The above list contains most of the substances which would be used to make isotonic solutions, and a little judgment will suffice to gauge the amount to be used in any particular case. Allowance must be made, of course, for the influence of the active ingredient on osmosis.

A more accurate method is that given by Dr. F. Nicola (*Giorn. arm. chim.*, through *Chem. Abst.*, 1921, 3120) who calculates first the tonicity of the active ingredient, then the amount of other salt or substance needed to produce an isotonic solution. Dr. Nicola uses **three factors in the calculations**, namely, (1) the **percentage strength** of solution expressed as weight-volume, (2) the **molecular weights** of the salts or compounds used, and (3) the approximate **dissociation constants** of the ingredients. From these he establishes an isotonic factor which is constant for each type of solution.

The isotonic factor for hypodermic solution is obtained as follows, based on the strength of the U. S. P. Physiological Salt Solution:

$$\frac{0.85(\text{Gm. NaCl in } 100 \text{ cc.})}{58.5(\text{mol. wt. NaCl})} = 0.01453$$

$$\text{then } 0.01453 \times 1.86 (\text{diss. const.}) = 0.027026.$$

All solutions intended for injection into the blood stream are to be based on this *serum-isotonic factor*, 0.027026.

The collyrium factor is similarly calculated:

$$\frac{1.4(\text{Gm. NaCl in } 100 \text{ cc.})}{58.5(\text{mol. wt. NaCl})} = 0.02393$$

then $0.02393 \times 1.80(\text{diss. const.}) = 0.04307$.

All solutions intended for **application to the eyes** are to be based on this **tear-isotonic factor**, 0.04307.

The dissociation constants will vary with different salts and also with different dilutions, but for practical purposes the following constants can be used. Sodium chloride being more generally used than any other salt is calculated on the tone-constant for the dilution used, namely, 1.86 for injections and 1.80 for collyria. Other salts are approximated as follows:

For **non-electrolytes** and weak electrolytes, such as sugars, gums, gelatin, tannin, boric acid, borax, alkali phosphates, citrates, acetates and bicarbonates, the **constant is 1.0**; for salts which **dissociate into two ions**, such as alkali chlorides, iodides and bromides, silver nitrate, zinc sulphate, etc., the **constant is 1.5**; for salts which **dissociate into three ions**, such as the chlorides, bromides and iodides of calcium, zinc, or copper, sodium sulphate, alum, etc., the **constant is 2.0**; and for salts which dissociate into **four ions**, such as ferric chloride, aluminum chloride, etc., the **constant is 2.5**.

The following examples will illustrate the method of calculation, employing these factors:

A 1 per cent solution of cocaine hydrochloride made isotonic for hypodermic injection.

$$\frac{1(\text{per cent})}{339.5(\text{mol. wt.})} \times 1.5 (\text{diss. const.}) = 0.00442$$

Factor $0.027026 - 0.00442 = 0.022606$ (differential factor)

$0.022606 \times 58.5 = 1.32245 \div 1.86 = 0.71$

Then 0.71 Gm. of sodium chloride must be added to each 100 cc. of a 1 per cent solution of cocaine hydrochloride to render it isotonic with blood serum.

A 1 per cent solution of cocaine hydrochloride made into an isotonic collyrium.

$$\frac{1}{339.5} \times 1.5 = 0.00442$$

Factor $0.04307 - 0.00442 = 0.03865$ (differential factor)

$0.03865 \times 58.5 = 2.255175 \div 1.8 = 1.25$

Then 1.25 Gm. of sodium chloride is to be added to each 100 cc. of 1 per cent solution of cocaine hydrochloride to make it isotonic with the lachrymal secretion.

A 1 per cent solution of cocaine hydrochloride made isotonic with boric acid for a collyrium.

$$\frac{1}{339.5} \times 1.5 = 0.00442$$

Factor $0.04307 - 0.00442 = 0.03865$ (differential factor)
 $0.03865 \times 62 = 2.39 \div 1 = 2.39$ Gm. of boric acid to be added to each 100 cc.

A 0.1 per cent solution of silver nitrate made isotonic with sodium nitrate for a collyrium.

A solution as weak as 0.1 per cent (1 in 1000) may be considered as having no tonicity factor.

Then:

Factor 0.04307×85 (mol. wt. $\text{NaNO}_3 = 3.6609$
 $3.6609 \div 1.5$ (diss. const.) = 2.44 Gm. of sodium nitrate to be added to 100 cc.

A 0.5 per cent solution of zinc sulphate made isotonic with sugar for a collyrium.

$$\frac{0.5}{287.5} = 0.001739 \times 1.5 = 0.0026$$

Factor $0.04307 - 0.0026 = 0.04047$ (differential factor)
 $0.04047 \times 342 \div 1 = 13.84$ Gm. of sugar per 100 cc.

Hypertonic solutions are more apt to produce local irritation, or even severe systemic reactions than hypotonic solutions. This is particularly true of solutions which are used intravenously. In the administration of arsphenamine, for instance the proper concentration of solution is a very important consideration to avoid severe reactions. But the technique of administration is also very important.

Prescriptions

- 1

R. Argenti nitratis.....	2.2	Dissolve the gelatin and afterwards
Potassii iodid.....	2.2	the potassium iodide in 50 cc. of hot
Gelatin.....	0.3	water and allow to cool. Dissolve the
Aquæ dest.....	100.0	silver nitrate in 50 cc. of cold distilled
M. Ft. sol. Sig.—Silver iodide for		water and add to the first solution
injection.		<i>slowly</i> with gentle shaking. (Thum.)
- 2

R. Argento-protein mitis... gr. xlviii		Sprinkle the silver proteinate on the
Aquæ destillat.....	3 ii	surface of the water contained in a
M. Ft. sol.		graduate and stir until dissolved. Or
		triturate the silver proteinate with
		a drachm of glycerin, then add the
		water and stir until dissolved.
- 3

1—Silver nitrate.....	27.6 grs.	Mix the two solutions <i>slowly</i> , let
Distilled water.....	1 quart	stand 24 hours, then heat on a steam
Make a solution.		bath for 48 hours, cool and decant the
2—Peptone.....	300 grs.	clear solution.
Sodium chloride.....	800 grs.	
Distilled water.....	1 quart	
Dissolve by aid of heat.		
Sig.—Colloidal silver chloride		
- 4

R. Caffeinæ sodio-benzoat	27.5 Gm.	Dissolve, filter and sterilize at 60° C.
Aquæ dest. sterilizat..	110.0 cc.	(N. F. V.)
M. Ft. solut. pro ampulla.		

- 5
 R. Quininae et ureae hydrochlor. 55 Gm.
 Aquae dest. sterilizat ad 110 cc.
 M. Ft. sol. pro ampulla.
 Dissolve and sterilize by heat at 60° C. (N. F. V.)
- 6
 R. Camphor. 11 Gm.
 Sterilized, nearly-neutral cottonseed oil, to make. . 55 cc.
 For ampul use.
 Sterilize the cottonseed oil by heating to 120° C. for one hour, in a suitable flask, cool to or below 60° C. and dissolve the camphor in sufficient of the sterilized oil in a sterile flask, to make 55 cc. of solution. Filter if necessary. (N. F. V.)
- 7
 R. Emetinae hydrochlorid 3.3 Gm.
 Liq. acidi hydrochlor. q. s.
 Liq. sodii chlorid physiol. ad. 110 cc.
 M. Ft. sol. pro ampulla.
 Dissolve the emetine hydrochloride in sufficient physiological salt solution to make 100 cc. Titrate 5 cc. of this with fiftieth-normal sodium hydroxide, using phenolphthalein T. S. as indicator, and to the remaining 95 cc. of solution add sufficient normal hydrochloric acid and water to make 105 cc. of solution which will contain 0.01 per cent of free hydrochloric acid. (N. F. V.)
- 8
 R. Sodii cacodylatis. 33 Gm.
 Aquae destillat sterilizat ad. 110 cc.
 M. Ft. solut. pro ampulla.
 Dissolve the sodium cacodylate in sufficient sterilized distilled water to make 110 cc. of solution. To 5 cc. of this, add 0.5 cc. of phenolphthalein T. S. and adjust the reaction to a slight pink by the addition of hydrochloric acid or of sodium carbonate, noting the amounts needed. Then add to the remaining solution a corresponding amount of acid or of sodium carbonate to produce a corresponding reaction. This solution should have a pH value of about 8.4. Filter and sterilize by heat at 100° C. (N. F. V.)
- 9
 R. Quininae dihydrochlor. . 55 Gm.
 Aquae destill. sterilizat. . 110 cc.
 M. Ft. sol. pro ampulla.
 Adjust the solution, after titrating a 1 cc. sample, by addition of hydrochloric acid, so that 1 cc. of the adjusted and finished solution will require 12.6 cc. of tenth normal sodium hydroxide to neutralize it, using phenolphthalein T. S. as indicator. Filter, and sterilize by heat at 100° C. (N. F. V.)
- 10
 R. Petrolati albi. 9.5
 Ung. hydrargyri fort. 1.0
 Hydrargyri. 19.5
 Petrolati liquidi. 20.0
 M. s. a. Sig.—Gray oil, for injection.
 (Oleum cinereum.)
 Triturate the mercury with the mercury ointment and 2.5 Gm. of white petrolatum until the mercury is extinguished, then add the rest of the ingredients.

11

- R. Ergotinæ..... gr. xv
 Phenolis..... gr. iss
 Aquæ destillat..... m lxxv
 M. solve et filtra. Sig.—For
 hypodermic injection.

12

- R. Thiosinamin..... ʒ iss
 Aquæ destillat..... ʒ ii
 M. Ft. sol. Sig.—For injection.

Thiosinamin is insoluble in water but will dissolve in a solution of antipyrine. In this case the physician allowed the use of sufficient antipyrine to make a solution. The solution should be sterile, and the addition of 0.4 per cent of cresol is advisable ordinarily.

13

- R. Cocainæ hydrochlor..... 0.500
 Sodii chlorid..... 0.625
 Aquæ destillat..... ad. 50.000
 M. Ft. collyr. Sig.—Isotonic cocaine
 collyrium.

14

- R. Zinci sulphatis..... 0.500
 Sodii sulphatis..... 1.350
 Aquæ destillat..... ad. 50.000
 M. Ft. collyr. Sig.—Isotonic zinc
 sulphate collyrium.

15

- R. Argenti nitratis..... 0.500
 Sodii nitratis..... 0.775
 Aquæ destillat..... ad. 50.000
 M. Ft. collyr. Sig.—Isotonic silver
 nitrate collyrium.

16

- R. Hydrargyri purificat..... 40.0
 Adipis lanæ..... 26.0
 Petrolati liquidi..... 60.0
 M. Ft. emulsionis. Sig.—Gray Oil.
 (Military formula.)

17

- R. Guaiacol..... 4 Gm.
 Iodoform..... 1 Gm.
 Olive oil to make..... 100 cc.
 For ampuls.

Sterilize about 100 cc. of olive oil by heat. Dissolve the guaiacol and iodoform in about 95 cc. of the sterilized and warm oil, by gentle agitation in a 3 oz. bottle which will have as little air-space as possible, make up to 100 cc. and filter with as little exposure to air as possible. This solution oxidizes and darkens readily.

State Board Prescriptions

1

- R. Tinct. ferri chlor..... ʒ iii
 Tinct. guaiaci ammon..... ʒ iv
 Tinct. aloes..... ʒ iv
 Syrupi..... ad. ʒ iv
 M. (La.)

2

- R. Caffeinæ citrat..... gr. xl
 Infus. digitalis..... ʒ iii
 Liq. ferr et ammon acet ad. ʒ viii
 M. Sig.—ʒ ii in water 3 times a day.
 Fla.

3

- R. Menthol..... gr. v
 Camphoræ..... gr. v
 Cocainæ mur..... gr. v
 Liq. petrolati..... ʒ ii
 M. Ft. sol. Sig.—Use as spray.
 (Fla.)

CHAPTER VI

EMULSIONS

An emulsion may be defined as an intimate mixture of immiscible fluids by means of some intermediate agent.

They are mostly milky-appearing mixtures, usually somewhat viscid, and often separate into two layers on standing. The term is usually applied to mixtures of oily, fatty, waxy or resinous bodies with water, but is also applied to intimate milky mixtures of fluids which are insoluble in each other (as chloroform, benzine, etc., with water), or sometimes to the suspension of an insoluble powder in water by means of an emulsifying agent.

Among the many branches of extemporaneous pharmacy, perhaps none is more of a bugbear to the average dispenser than the making of emulsions. If he be ignorant of the principles and rules governing emulsification, he quickly comes to look upon them as unstable mixtures of uncertain composition obtained by chance or unlimited muscle used in triturating or agitating.

The making of an emulsion, with a proper emulsifying agent, is, however, almost as positive and certain an operation as the making of a 50 per cent solution of a salt, or of any other simple mixture.

Let us first consider **the theory of emulsification**, then the practical operations involved in making emulsions of different kinds.

If we place half an ounce of a fixed oil, as cod-liver oil, in a two-ounce bottle, add to it half an ounce of water and shake vigorously, the oil is broken up into globules and diffused through the water, and the mixture has an opaque appearance. On discontinuing the agitation, however, the oil and water quickly separate into layers again.

If now we place in another two-ounce bottle half an ounce of mucilage of acacia, turn the bottle so as to flow the mucilage around the inner sides, then add half an ounce of oil and shake vigorously, we obtain a whiter and more opaque mixture than before, which remains permanent for a period varying with the condition of the oil, the density of the mucilage, and the vigor of the shaking which we have given to it.

Here we have broken up the globules of oil as before, but the globules are much smaller than in the first experiment, and the mucilage promotes an adhesion between the oil and the water in the mucilage and an emulsion ensues, although the difference in the specific gravities of the two liquids is greater than before.

It will be noticed that when the oil and water are shaken together, the oil is broken up much more than the water, or in other words the oil forms much smaller globules than the water. But when the mucilage is used, there is no perceptible difference in the sizes of the oil and the aqueous globules. This can be seen more readily by

dropping water slowly into a column of oil, and into another portion of oil dropping mucilage of acacia, when it may be easily observed that the mucilage forms smaller drops than the water.

To secure a permanent emulsion of an oil then, two things are necessary: first to **get the oil into very minute globules**, and second to **prevent these globules from coalescing on standing**. The size of the globules, in any liquid, depends partly upon the vigor of the agitation, but more upon what is known as surface tension, or the cohesive properties of the liquid. Water has a higher surface tension than most other liquids, and so tends to form larger drops or globules, and a substance which will reduce its surface tension is needed. Then to prevent these small globules from running together and coalescing, first into larger globules and finally into separate fluids, some means must be employed to impart adhesion between the oil and water surfaces, so that they will remain in intimate contact.

The gum of the mucilage imparts both these properties to the water. It reduces the surface tension, and so forms smaller droplets of water, and it creates an adhesion between the oil and water surfaces that is stronger than the cohesive properties of either. If, in addition to this, it makes the water more viscous, that is an added advantage in securing permanency.

Emulsifying agents also form a film or coating around the oil globules, which prevents their coalescing.

A substance which lowers the surface tension of a liquid tends to concentrate at the surface or interface of that liquid. This means that in an emulsion, the film which immediately surrounds a globule of oil, or other emulsified body, is much stronger in emulsifying agent than the body of the solution. The agent flows to and concentrates around the globules, and this is a large factor in preventing their coalescence. This is true of all emulsifying agents. In some cases evidence has been found that the emulsifying agent surrounds the globule with a layer one molecule thick in which the molecules are "oriented" or arranged according to their axis and physical affinities. That is, the end or group in the molecule which tends to dissolve in water is toward the water side of the film, while the group in the molecule which tends to dissolve in oil is on the oil side. The molecules thus act as a kind of bridge to keep the oil and water in physical connection.

Another important factor in preventing the coalescence of the globules is that the oil and the water are both electrically charged, but unevenly charged, with the same polarity of electrical energy. They thus tend to repel each other, and to remain in globular form.

Two important factors in the stability of emulsions are therefore the film-covering of the globules, and the electrical energy which repels the globules from each other.

The permanence of an emulsion consists in obtaining the globules in so fine a condition that even a very thin mucilage can prevent their coalescing. These globules are ordinarily too small to be seen with the naked eye, but in emulsions made with a thick mucilage, as mucilage of tragacanth, or mucilage of Irish moss, the globules of oil may be distinctly visible to the eye and yet the emulsion remain quite stable, owing to the viscosity of the mucilage which envelops them. Such emulsions, however, will not bear very much dilution.

The most exacting part of emulsion-making lies in getting the emulsion started. Thus, in making a pint of 50 per cent emulsion it would be extremely difficult, if not impossible, to do it all in one operation, but by emulsifying a portion or the whole of the oil with a portion of the water and the emulsifying agent, we get a *primary emulsion* which can be diluted with oil, water or other solutions as desired.

Good emulsions often separate into layers after standing, but without showing any separated oil. An emulsion should not be condemned for this, because the separation is due not to faulty manipulation in making the emulsion, or to improper ingredients or proportions therein, but to excess of dilution, and a little shaking will quickly rediffuse it. The same thing occurs in milk—the best type of a natural emulsion—in which the true emulsion portion separates as cream. When separation of this *emulsion* occurs, we obtain the fat as butter.

In triturating an emulsion, no pressure is needed, but a rapid motion is essential. Five minutes of very rapid trituration will accomplish more in emulsifying an oil or balsam, than an hour of slow trituration. Indeed, if after five minutes or less of rapid trituration an oil does not emulsify, it is good evidence of some fault in the ingredients used, or of their proportions, and a satisfactory emulsion cannot be expected without alteration of the ingredients. This refers, of course, to small quantities of emulsion, involving a pint or less of oil. Large quantities require longer trituration.

The pestle should be held loosely between the thumb and first two or three fingers, and the motion imparted to it by means of the fingers and wrist, as well as those of the arm and shoulder. This will be found much less tiresome than when the pestle is grasped firmly with the whole hand, and the motion imparted from the arm and shoulder alone. The mortar should be of a capacity three to four times that of the quantity of emulsion which is being made, but the emulsion should be slopped up upon the sides as little as possible. Glass mortars are not suitable, the surface being too smooth. The emulsion may be stirred in either direction, or alternately.

Emulsifying machines are apparatuses for mechanical agitation. The smaller, hand machines are usually an application of the Dover egg-beater in an enlarged form. For small quantities of emulsions, an egg-beater of any kind is an efficient substitute. The larger machines are more in line with the butter-churn, and indeed a churn is an excellent emulsion-machine. The principle of these is well imitated by a female piston-syringe, the oil and water mixture being repeatedly drawn into and forced out of the syringe, thus churning them together. All such appliances aid emulsification by breaking up the globules, and an egg-beater or a piston-syringe may be easier to use than a mortar, and will often accomplish results that cannot be secured in the mortar.

For making small quantities of emulsions, up to a pint or twenty fluid ounces at a time, the electrical mixer which is used at soda fountains for mixing drinks, and of which the Arnold Automatic Mixer is a type, is an excellent appliance. It is rapid in action, easily cleaned, materials can be added while in operation, and it makes very satisfactory emulsions with very little labor or attention.

All emulsifiable bodies do not emulsify with equal ease. Fixed oils, as cod-liver oil, castor oil, seed oils, etc., emulsify more readily than volatile oils, as turpentine oil, the fragrant oils, etc. when acacia or other gum is used. Emulsifying agents differ also in their power to emulsify different kinds of oils. Many bodies, as creosote, camphor, some oleoresins, phosphorus, etc., cannot easily be emulsified alone, but can readily be made into an emulsion if first dissolved in a fixed

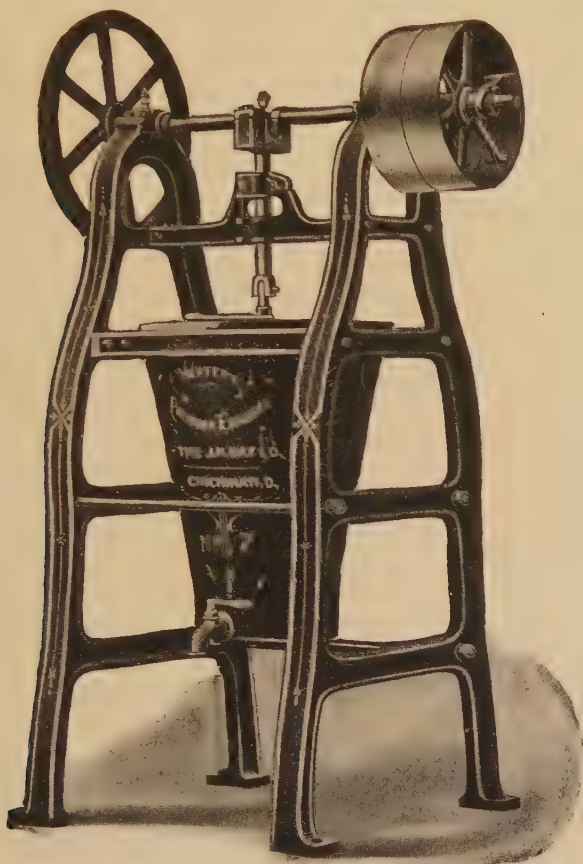


FIG. 7.—Hunter's pneumatic emulsifier.

oil, which is then emulsified. Almond oil (sweet) is an excellent solvent for this purpose, being bland and seldom rancid.

Heat will sometimes prevent the union of an emulsion. This is not liable to occur, though, except in cases where artificial heat has been employed. Petroleum oil emulsifies more easily when warm.

Some salts tend strongly to break emulsions, and cannot be incorporated except in small amounts. A few salts aid in emulsification in small amounts, but tend to break the emulsion if used freely. A similar condition is observed with some neutral bodies.

Neutral salts of ammonium, (particularly the nitrate, chloride and bromide) of potassium, sodium and lithium are generally compatible with emulsions except in excessive amounts.

Salts of calcium and magnesium must be added more cautiously, but are compatible to a considerable extent, while salts of strontium have a stronger tendency to break the emulsion.

Salts of aluminum, iron, copper, zinc, lead, mercury, bismuth etc. have a strong tendency to break emulsions, and must be added very cautiously and in small proportions. The more acid the salt, and the higher its equivalent the greater is the influence upon the emulsion. This applies especially to the soluble, normal salts. Insoluble salts can be suspended in emulsions, and when not hydrolysed by the water or chemically influenced by the emulsifying agent they display little influence upon the emulsion.

Alcohol, glycerin and syrup cannot be used in making emulsions, but may be used to dilute it. Alcohol is compatible, in small proportions only—usually below 25 per cent of the total volume. Alcohol in excess precipitates gums, albuminous bodies and other emulsifying agents and will thus destroy the emulsion. But in small proportions—usually 7 to 10 per cent it preserves emulsions by preventing fermentation or bacterial change.

Glycerin has less of a destructive action, and helps to stabilize emulsions by adding to the viscosity. Syrup also hinders separation, if not in excess, and so aids in the permanency of the emulsion.

Salt solutions, alcohol or syrup should be added to the emulsion after emulsification has been accomplished. If the formula will admit of further dilution with water, this should be done and the salt solution, alcohol etc. added last and also introduced gradually, with active agitation to mix it quickly. If separation of the emulsion threatens, a very little water may prevent, or restore it.

Alkaline salts sometimes aid in making emulsions, but when combined in an emulsion made with a gum or an albuminous agent, an alkaline salt may act in a way that is contrary to that of the agent and so break the emulsion. Combinations of emulsifying agents must be of the same type to act together, otherwise they may interfere with each other.

Two types of emulsions are made: one in which oil is dispersed in water, and one in which water is dispersed in oil. In the first case the oil is the liquid that is emulsified and the water is the liquid in which it is distributed. The other case is the reverse. In the first instance the oil is described as the "dispersed phase" and the water as the "continuous phase."

The emulsifying agent determines which type shall result. When the emulsifying agent is soluble in water—or in case of an insoluble agent is more easily wetted by water than by oil—an oil-in-water emulsion is obtained. When the emulsifying agent is soluble in oil, or more easily wetted by oil, a water-in-oil emulsion results. The two types look alike in so far as physical appearance is concerned, but they differ somewhat in properties. The oil-in-water emulsion can be diluted with water without breaking, but not with oil (except to a limited extent) while the water-in-oil type can be diluted with

oil but not (much) with water. This is a means of distinguishing between the two.

Most pharmaceutical emulsions, especially those that are labelled "emulsion"—are of the first type—oil-in-water. But there are some preparations in common use in pharmacy that belong to the second type,—linimentum calcis, for instance.

The proportion of oil to water is not the essential factor. Emulsions of oil-in-water have been prepared containing 99 per cent of oil in 1 per cent of a water solution of soap, and are still oil-in-water emulsions. The character of the emulsifying agent is the determining factor.

EMULSIFYING AGENTS

As before mentioned, emulsifying agents are bodies that, when dissolved in water, reduce the surface tension of water and so make smaller droplets; and then coat the droplets of oil with a film which prevents coalescing; and they also promote adhesion. Many of them also make a viscous solution, which is of much advantage in securing permanency. Viscous bodies flow slowly, and thus in a mixture will separate more slowly. It is for this reason that viscid agents are preferred for emulsions that are to be kept in stock, and are often used for this purpose though poor emulsifying agents.

It will be further noticed that *bodies which produce foam in watery fluids are usually good emulsifying agents.*

The emulsifying agents used in pharmacy are chiefly albuminous, mucilaginous, saponaceous or colloidal in character.

ALBUMINOUS AGENTS

The albuminous agents are **characterized by** ease of manipulation, wide range of power, and palatability, but they do not keep well, and emulsions made with them soon spoil unless preserved by some antiseptic.

In milk and yolk of egg we have good examples of emulsions with an albuminous agent; milk being an emulsion of butter fat with *casein*, and yolk of egg an emulsion of a peculiar fat with *vitellin*.

Both **Milk** and **Yolk of Egg** are used as emulsifying agents and are unexcelled as such except as regards keeping qualities. The propensities of milk to "sour" and of egg to become "stale" are well known, and these propensities are not changed by combining with them other fats or oils. But for emulsions which are to be taken immediately, nothing equals these agents for ease of manipulation or palatableness. The addition of about 10 percent. of alcohol, preferably in the form of brandy, will preserve them for a time.

It has already been stated that it is much easier to dilute an emulsion already formed with additional oil or water, than to form an emulsion primarily. Both milk and yolk of egg being natural emulsions, we would, therefore, expect that they would be easy of manipulation when used as emulsifying agents. Not only is this true, but they also emulsify successfully a larger variety of fatty bodies than most other agents.

Milk, as ordinarily obtained, is seldom used except as a diluent. In this capacity it serves well for covering the taste of sharp or acrid,

bodies, as tinctures of capsicum, ginger, etc., and for many salts, chloral, etc. It is too weak of itself to be used to any extent as an emulsifying agent. The ordinary condensed milk of the market serves in this capacity admirably. This contains some sugar, which however, does not interfere. In using it, the condensed milk is diluted with an equal bulk of water, then the oil is added in small portions, constantly triturating. An emulsion containing 84 per cent of oil has been obtained by combining $6\frac{3}{4}$ ounces of cod-liver oil with 5 drachms of condensed milk, previously diluted with 5 drachms of water. This emulsion was of the consistency of lard, and kept well for a month.

Weaker emulsions may be obtained from the same mixture of condensed milk and water, by emulsifying a sufficient quantity of

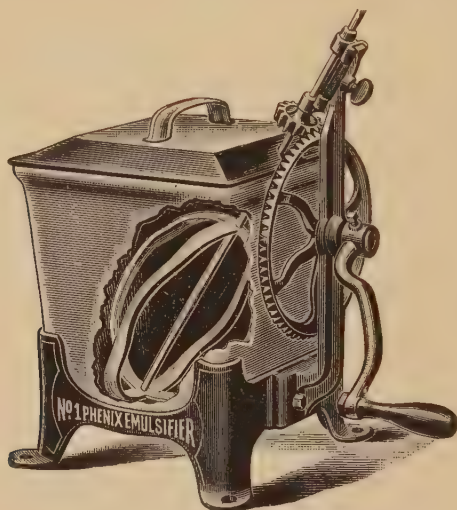


FIG. 8.—Phenix emulsifier.

oil, then adding water gradually until the required bulk is obtained. These weaker emulsions do not keep as long as the stronger ones.

Glycerite of yolk of egg is an excellent form of the second to use. The oil should be added in portions to the glycerite in a capacious mortar, with constant trituration, and lastly the diluent may be added in the same manner. Both of these agents are used with excellent results for other bodies more difficult to emulsify than oils, such as creosote, chloroform, terebene, oleoresins, balsams, resinous tinctures, etc.

The appearance of the emulsion will depend largely upon the condition of the egg. When quite fresh, yolk of egg yields a creamy white emulsion which shows no tendency to separate, but with old eggs, though they may show no signs of becoming stale, the emulsion is decidedly yellow, and in some cases may be deeply so.

For ease of manipulation, for palatableness, and for general utility, yolk of egg and condensed milk stand first among emulsifying agents. Their tendency to spoil, however, limits them for general

use, since emulsions made with either seldom remain palatable for more than a few days, unless a preservative is added. They have a special value, however, in emulsions of chloroform, creosote, and other antiseptic bodies, the preservative properties of which will prevent any change for several weeks.

Less used albuminous agents are the following:

Casein has been recommended as an emulsifying agent. It is, however, not easily obtained, and when procured possesses no advantage over acacia, so far as ease of manipulation is concerned.

It should be comparatively fresh, since it decomposes on standing. The moist (freshly precipitated and undried) casein, with a little sodium bicarbonate, gives the best results.

The dry casein is best prepared from skimmed (by centrifugal force) **milk**, since it is almost impossible to separate the fat from it when it is prepared from unskimmed milk. The skimmed milk can be easily obtained in all large cities and is also much cheaper. The casein is obtained by first adding ammonia water to the milk (about two fluidounces to a gallon) and allowing to stand 24 hours. Any creamy layer which has separated is then removed, and the casein precipitated from the serum by a slight excess of acetic acid. The magma is then collected and pressed, mixed with one-tenth its weight of sodium bicarbonate and dried at a gentle heat. (Too high a heat destroys it.) When thoroughly dried it is powdered and mixed with enough sugar of milk to make a 10 per cent mixture of casein.

This mixture may be used for emulsifying in the same manner and proportions as powdered acacia, but does not yield as good results.

Pancreatin is a digestive body obtained from the pancreas of the hog. It consists of an albuminous body similar to casein and four fermentative bodies, one of which has the power of digesting or decomposing fats and oils. It is always used in alkaline solutions, being decomposed by acids.

It may be used as an emulsifying agent in two ways: either by making a strong aqueous solution with which the oil is gradually combined, as in mucilage of acacia, or by warming the aqueous solution, at about 125° F., with the oil until the latter is partially digested.

By the latter method the oil is partially decomposed, and the resulting mixture is not properly an emulsion, although having the appearance of one. If heated too high the pancreatin will be decomposed.

Pancreatin is not a uniform body, and its emulsifying and digesting powers will be found to vary considerably.

Good pancreatin should emulsify eight to ten times its weight of cod-liver oil by the first method. It is not a good agent for emulsifying volatile oils.

ALBUMINOUS AND MUCILAGINOUS AGENTS

A few bodies suitable for emulsifying are both gummy and albuminous in character.

Most prominent among these are certain seeds and Irish moss.

Most fleshy seeds contain a fixed oil associated with gummy and albuminous matter, and form an emulsion when deprived of their skins and beaten up with water. Pumpkin seed is sometimes dis-

pensed in this manner. The skins may be removed by plunging first into hot water for a minute, then into cold, whereby the skin becomes loosened and may be slipped off. This is called "blanching" the seeds.

In almonds—a favorite seed for emulsions—there exists, in connection with the gum, a principle called *emulsin*, which assists in forming a smooth emulsion. This is partially destroyed by boiling water, and a better way of blanching almonds, when time will allow, is to soak the seeds for half an hour, or until the skins are loosened in lukewarm water. Almonds have the advantage of adding flavor as well as emulsifying. In many other seeds there is found a ferment similar to emulsin which aids in emulsifying the oil. Hence hot water should be avoided in making seed emulsions.

In rubbing the seeds to a pulp a little water should be first added (about one part to ten parts of seed), since the pressure may force oil out of them if sufficient water is not present. The seeds should then be rubbed to a smooth, creamy paste, free from all lumps or gritty particles.

After diluting until quite fluid the liquid may be strained, if necessary. Seeds which contain a large proportion of gum may be used as emulsifying agents.

Mucilage of Irish Moss has had some favor as an emulsifying agent. Its chief function is to impart viscosity and prevent separation of an aqueous layer in emulsions. It is not in itself a good emulsifying agent, and so is not much used alone, but possesses many advantages in economy and compatibility when used in combination with other emulsifying agents. It requires much more trituration than other agents, and does not yield as white and creamy an emulsion, commonly showing fine oil globules. The emulsion, however, does not separate for some time when well made. This oily appearance can be avoided by first emulsifying a portion of the oil with another emulsifying agent, and using the mucilage of Irish moss as a diluent rather than as an emulsifying agent. Neither the mucilage nor emulsions made from it keep well unless a preservative agent is added. The albuminous matter quickly ferments and putrefaction commences, giving off ill-smelling gases. This can be retarded for a long period or prevented altogether by substituting alcohol for about a quarter of the water used in making the mucilage, or by substituting alcohol for a part of the water in diluting the emulsion.

Glycerin appears to aid rather than hinder its emulsifying powers. The mucilage of the National Formulary is quite thin. A much whiter and better emulsion can be made with a mucilage 50 per cent stronger.

Emulsions with Irish moss can also be made easier and of a better appearance by addition of a little primary emulsion made with acacia or other emulsifying agent to the mucilage. Thus, in making a pint of emulsion, if half an ounce of the oil be emulsified first with $\frac{3}{4}$ acacia, and this emulsion mixed with the mucilage of Irish moss, the oil afterward added will emulsify quicker and be whiter in appearance. The addition of two or three drops of solution of potassa to the mucilage, just sufficient to neutralize the acid present, also improves its emulsi-

fying powers. A 90 per cent emulsion of cod-liver oil can be made by using a mixture of equal parts of mucilage of Irish moss and condensed milk. The mucilage of Irish moss for this should be double the strength of the National Formulary mucilage, or 24 grains of moss to an ounce of mucilage. This emulsion does not keep as well as the 84 per cent emulsion made with condensed milk and water. In making mucilage of Irish moss, only bright succulent pieces should be selected and the boiling continued for at least fifteen minutes. It should be boiled very gently in a capacious vessel to prevent frothing over. Irish moss is more easily combined with tincture of iron and acid than the mucilaginous agents.

Gelatin is albuminous only, and is recommended chiefly as an emulsifier of petroleum oils. Gelatin emulsifies liquid petrolatum more easily than other oils, and makes a very satisfactory appearing emulsion. But the emulsions with gelatin are difficult to keep from spoiling, which limits their value. It resembles mucilage of Irish moss in properties and keeping qualities. Its best recommendation is its low cost. It may be used combined with alkaline salts or soft soap, in veterinary practice, etc.

Agar-agar has come into use as an emulsifying agent for heavy liquid petrolatum. Since both are used as mechanical regulators for the bowels, the combination sounds good. Agar-agar is so nearly insoluble that its emulsifying properties are obtained more as an insoluble colloid than as an albuminous agent. The agar is used as a very fine powder, and is soaked in cold water for a few hours before being employed for emulsifying. Only enough water is used to cover it well and to supply the moisture needed to thoroughly swell it. The oil is then triturated with the wet agar, using small portions at a time, and alternating with water as the emulsion shows signs of breaking.

Some of the commercial emulsions with agar contain acacia also as the emulsifying agent. Agar alone is not very satisfactory for the purpose. If more than about 1.5 Gm. of agar per 100 cc. of emulsion is used, a buff or grayish colored emulsion is obtained instead of white. In that proportion but a small amount of oil can be emulsified, so another agent is employed to obtain a presentable emulsion containing sufficient of the oil to be acceptable. Agar makes a smooth and white emulsion with liquid petrolatum, but its usefulness is very limited.

Professor Saalbach recommends that agar emulsions be made by first making the mucilage of agar. One gram of agar is boiled in 80 cc. of water until the agar is completely dissolved, the solution allowed to cool, and the jelly mixed with 80 cc. of oil and churned in an electric mixer until a smooth white emulsion is obtained. Fifteen minutes or more of churning is required.

MUCILAGINOUS AGENTS

Gums or mucilaginous bodies are, as a class, the best for general use in pharmaceutical emulsions.

They are capable of emulsifying well all bodies desired in emulsions, and the resulting emulsion keeps well under ordinary conditions. All true gums can be used as emulsifying agents. They form very fine, white emulsions.

Alkalies and borax must be added very cautiously to gum emulsions, since they tend to saponify the oil and break the emulsion. Borax also coagulates gums, but this can be prevented by the addition of sugar.

Gums-resins (ammoniac, asafoetida, myrrh, etc.) **form natural emulsions** when mixed with water. They consist of a gum associated with an oleoresin, and are never used as emulsifying *agents*, but are excellent types of gum-emulsions. When made from the whole drug they are milky in appearance, but if the powdered drug be used a dirty-brown mixture results, which quickly deposits a granular sediment, and leaves an almost clear, watery liquid. This is because the commercial powders are made from garblings, and these are further injured by long heating, which drives out most of the volatile oil, and completely changes the character of the drug. *Gum-resins cannot be powdered in large quantities without loss of their most valuable constituents.*

Small quantities of powder may be obtained for immediate use by taking advantage of the fact that extreme cold makes them brittle, and rubbing slowly in a well-chilled mortar and in cold air. The powder thus obtained will cake together again when it becomes warm.

The emulsions can be easily formed at ordinary temperatures by rubbing the *selected* pieces of drug with successive portions of water until all lumps are obliterated.

Acacia is the emulsifying-agent par excellence for general use. Emulsions made with it are attractive in appearance, palatable and permanent. Its range of power is exceeded only by the albuminous agents mentioned. Emulsions of chloroform, oleoresins, resinous tinctures, etc., can be made readily with acacia, but separate into layers quicker than when made with yolk of egg.

Either dry acacia or mucilage of acacia can be used for emulsions. Both have their advocates in point of preference, but dry acacia has proved itself a quicker and more certain agent to use, at least in the hands of novices. This is probably due in part to the fact that dry acacia must always be used in definite proportions, as must also the water first added. Two rules are in common use for making emulsions with dry acacia.

Rule 1.—For one part of gum use four parts of fixed oil (or two parts of volatile oil), and once and a half as much water as gum.

Rule 2 varies only in using twice as much water as gum. This rule may be easily remembered as **the 1, 2, 4, rule.**—(Gum 1, water 2, oil 4.)

Exceptions of these may be met with in that the proportions of oil to gum vary with different oils; most fixed oils being emulsified well in proportion of four of oil to one of gum; while most volatile oils require one of gum to two of oil. Occasionally, however, a fixed oil is found which requires one third its weight of acacia, or a volatile body which requires an equal weight. The amount of dilution to which the primary emulsion is subject also affects the proportions. In all cases, once-and-a-half or twice as much water as gum must be used for the primary emulsion.

Suppose we wish to make a pint of 50 per cent (by volume) emulsion of cod liver oil.

This will require $\mathfrak{3}\text{ viij}$ of oil, and by the rules every four parts of oil (or $\mathfrak{3}\text{ iv}$) will require one part (or $\mathfrak{3}\text{ j}$) of gum; then the $\mathfrak{3}\text{ viij}$ of oil

requires ℥ij of gum. Carefully weigh, then, the ℥ij of powdered acacia, place it in a *dry* mortar, having a capacity of three or four pints, and pour in the f℥viij of cod-liver oil. Triturate lightly until the acacia is diffused evenly through the oil, which will be accomplished in about a minute, if both acacia and mortar were dry.

Now lift the pestle, and having carefully measured f℥iv of water (Rule 2), pour it all upon the oil in the center of the mortar, then triturate rapidly until a perfectly white creamy mixture results, showing no globules or color of oil, and which has a crackling sound when triturated. This is called a *primary emulsion*. Then add to this slowly, with constant trituration, water enough to make a pint of emulsion. This emulsion is of the color and consistence of thick cream, and is permanent.

Failure only results, in using this formula, from lack of care in measuring or weighing. *Approximate amounts will not do.* The acacia must be weighed accurately, and both the oil and water measured accurately and in clean graduates. Do not measure water or aqueous liquids in an oily graduate. The primary emulsion must always be made by means of oil, gum and *water*; *it cannot be made by using syrup, or a solution of a salt in place of the water.* Such solutions and other liquids can be incorporated with a primary emulsion, but cannot be used in making it. A failure will not occur when these precautions are observed.

The 50 per cent emulsions of the market, however, seldom, if ever, contain as much acacia as this. In making them, advantage is taken of the fact that **the primary emulsion will emulsify an additional amount of oil**, if properly combined, without "breaking." This enables us to make this emulsion, using only half the amount of acacia in the formula just given.

Thus, instead of mixing f℥viij of oil, ℥ij of acacia and f℥iv of water for our primary emulsion, we may take half of the required amount of oil, or f℥iv of cod-liver oil, ℥j of powdered acacia and f℥ij of water, and make a primary emulsion as before. Then to this primary emulsion add the remainder of the oil, in portions of ℥ij or ℥iij at a time alternating with portions of water ℥j or ℥iiss each, and triturating each portion until thoroughly emulsified before adding the next. Finally, enough water is added, in portions, to make the finished emulsion measure a pint. This requires but little more skill than the first method, and only half as much acacia, and makes a considerable saving in cost.

Success with powdered acacia appears to depend more upon an exact proportion between the oil and the water in forming the primary emulsion than upon the proportion of acacia used.

Thus a primary emulsion may be made with **one** part of gum, **four** of oil and **two** of water; or with **one** of gum, **six** of oil and **three** of water; or with **one** of gum, **eight** of oil and **four** of water. In each case it will be noticed that **exactly** half as much water as oil must be used. But it cannot be said that half as much water as oil must be employed in all cases, for in some cases a larger proportion of gum is needed, and the quantity of water must be sufficient to dissolve all the gum. The following statement may be depended upon in all cases:

RULE. When the proportion of gum used is one-fourth that of the oil, or less, use half as much water as oil; when the proportion of gum to oil is greater than one-fourth, use twice as much water as gum.

In using mucilage of acacia, the mucilage is placed in a dry mortar, and the oil added in small portions, each portion being thoroughly emulsified before adding the next. One ounce of mucilage will easily emulsify two ounces of cod-liver oil, with the addition of a little water near the end of the emulsification.

Often a failure is made in this through the breaking of the emulsion while adding the last portions of oil. A little calculation will show the cause. One ounce of mucilage contains 35 per cent weight-volume of gum, or about 170 grains. This amount of gum will emulsify, according to the rule, about 3xix of the oil. Then, after adding 3xix of oil to the mucilage, the remainder of the oil should be alternated with portions of water, half as much water as oil, as in making the 50 per cent emulsion.

Mucilage of acacia, when used for emulsions, must always be fresh. The slightest trace of sourness may prevent its forming an emulsion.

When other emulsifying agents are prescribed in combination with acacia, a mucilage may be made with the combined emulsifiers, and the oil gradually incorporated, or a primary emulsion may be made with the acacia and a part of the oil, to which are added first the other agents, then the remainder of the oil, with a little water if needed.

Acacia can be used to advantage in emulsifying resinous tinctures when mixed with aqueous fluids. The amount to use will vary somewhat with the strength of the tincture and the amount of dilution.

Tincture of benzoin, simple or compound, can generally be emulsified with half its volume of mucilage, while ammoniated tincture of guaiac requires nearly or quite its own volume of mucilage.

The mucilage should be diluted with water to prevent precipitation of gum in the mucilage by the alcohol in the tincture, then the tincture added gradually with constant trituration.

The addition of a little gum or mucilage to mixtures containing resinous tinctures, though not directed on the prescription, is often justifiable, and in the line of elegant pharmacy.

Wax, spermaceti, etc., may be emulsified by melting in a hot mortar, adding an equal weight of powdered acacia, then one-and-a-half times as much *hot* water, and triturating until a primary emulsion is formed, which may afterward be diluted with warm water. Yellow wax should be used, as it makes a better emulsion than the white. Copaiba requires one-third to one-half its weight of acacia. But soap or quillaja is preferred for wax and resinous bodies for emulsions which are to be used externally.

Tragacanth is, next to acacia, the most popular emulsifying agent. It is a type of the "insoluble gums," and consists of a small proportion of true gum which dissolves in water and forms a very tenacious mucilage, and a large proportion of *bassorin*, or insoluble gum, which swells enormously in water, but does not dissolve.

Thus a mucilage of tragacanth, if made by treating one part of the gum with twenty parts of water, is a thick, gelatinous semi-solid, which is capable of occluding a large amount of oil, the bassorin being an obstacle to coalescence rather than a good emulsifier for the oil.

It forms dense emulsions, which are not as white and creamy as those made with acacia, and will not bear as much dilution. Tragacanth is capable of emulsifying 40 to 50 times its weight of oil, but it is not often used alone, as the emulsions are too thick to be agreeable. It is frequently combined with acacia as a means of cheapening the emulsion, and also to prevent separation into layers by thickening it. For some reason, not understood, acacia liquefies a tragacanth emulsion, and the tragacanth must be used in large excess to be efficient. Various proportions of tragacanth and acacia may be made into a mucilage into which the oil is stirred, as in using mucilage of acacia. Mixtures of acacia and tragacanth are commonly used for commercial emulsions, and frequently are combined with starchy bodies. Thus equal parts of acacia, tragacanth and arrowroot make an excellent agent when used in the proportion of one part of mixture to 10 of oil.

In making an oil emulsion with tragacanth, a mucilage should be first formed into which the oil is gradually stirred as in using mucilage of acacia.

In emulsifying chloroform, resinous tinctures, and all alcoholic or ethereal fluids, the best results are obtained by placing the powdered tragacanth in a dry bottle, to which the fluid is added, and then, after shaking, about 20 times as much water as gum and the whole shaken vigorously. If oil is to be incorporated it must be added to this mucilage, and not to the dry gum.

Tragacanth is specially useful for suspending heavy powders, like bismuth subnitrate, etc., in mixtures. About 70 grains to a pint of mixture is sufficient, and it is best used after wetting the tragacanth well with half an ounce of alcohol, then adding the water.

Dextrin has been recommended by the National Formulary. Only white dextrin should be used, and this is difficult to obtain of good quality. Owing chiefly to this difficulty emulsions made with dextrin are now practically obsolete.

Extract of Malt is sometimes used as an emulsifying agent, and may be classed among the gummy agents, since it contains gum and some dextrin. The thick semi-solid extract is used for this purpose, the oil being added gradually to it in a warm mortar with trituration. It yields a brownish emulsion, which may separate into layers, but does not separate oil. Its taste is enhanced by the malt, and probably the action of the diastase is of value. It should not be used unless directed, however, since extract of malt has a therapeutic action of its own which may be undesirable. Extract of malt is frequently acid, which interferes with its emulsifying powers. The addition of a little bicarbonate of soda will correct this, and improve its effects. It is an excellent agent for cod-liver oil, and for resinous bodies like asafœtida (tincture), ammoniated tincture of guaiac, compound tincture of benzoin, etc. A moderate heat helps the emulsion to form.

Honey is a favorite emulsifying agent for resinous tinctures, with some pharmacists. It is preferred because it is both a flavoring and an emulsifying agent, and makes a more palatable mixture with such preparations as tincture of cannabis, tincture of guaiac, tincture of podopyllum etc. It is ordinarily used in equal volume with the tincture to be emulsified. Honey has slight emulsifying power over oils,

either fixed or volatile, but it often is a good adjuvant to emulsions made with other agents.

Extract of Licorice is also used. The powdered extract is usually employed, it being first triturated to a paste with water or (preferably) syrup, then the oil added gradually. It does not make a very fine emulsion, and oil globules are usually observable on close inspection. The emulsion must be made quite thick and stiff or separation of oil is likely to take place. It resembles tragacanth in its emulsifying efficiency, but being dark in color the coarseness of the emulsion is not so noticeable. It is one of the best agents to disguise the taste of cod-liver oil.

SAPONACEOUS AGENTS

These are of two kinds, the saponin emulsions, and the soaps. Emulsions with this class of agents are best made by shaking in a bottle. They are very easy to make, and are most desirable in emulsions of fats and waxes which are to be used externally, as in treatment of skin diseases, etc.

Quillaja, or soap-tree bark, contains a principle called saponin, which has the property of emulsifying oils and other bodies. It is this same principle which causes the frothing in preparations of sarsaparilla and senega.

Tincture of quillaja is one of the easiest emulsifying agents to use, and has a wide range of power, forming good emulsions with nearly all of the emulsifiable bodies. Even mercury may be emulsified (?) with it by gentle shaking. The usual *modus operandi* is to place the tincture in a dry bottle and add the oil to it in portions, shaking vigorously after each addition. The National Formulary formerly gave a formula for preparing an emulsion in this way containing 85 per cent of cod-liver oil, one part of the tincture emulsifying $8\frac{1}{2}$ parts of oil. Volatile oils require a much larger proportion of the tincture, sometimes an equal volume. Quillaja emulsions are usually more satisfactory when the proportion of oil in the emulsion is low.

Quillaja is especially useful in emulsions containing free acid, which interferes seriously with other emulsifying agents. Its acrid taste and irritating properties, however, which are noticeable in an emulsion, are a decided objection to it for internal use.

Tincture of Senega may be used in place of tincture of quillaja, and is less acrid. This is especially useful when an expectorant can be given with the oil, but should not be used when this is contraindicated.

Soaps and Alkalies.—Soap is seldom desirable for emulsions intended to be taken internally, but is often used for external preparations, as skin-creams, liniments, etc. A soap is a chemical combination of an alkali base with a fat or oil, the acids from the fat being combined with the alkali and a chemical salt or soap is formed. Soaps have the property of emulsifying additional portions of oil. Alkalies act in the same manner by first forming a soap with part of the oil, which then serves to emulsify more oil. Soaps are powerful emulsifying agents, particularly soft soaps. Soaps reduce the surface-tension of water very materially, a drop of pure water being $2\frac{1}{2}$ times as large

as a drop of a weak soap solution. Hence the emulsifying power of soap is very great.

While a weak solution of soap reduces the surface tension of water, a strong solution raises the tension, hence a strong soap solution is a less efficient emulsifier than a weak one. Indeed it is easily possible to break a soap emulsion by dissolving soap in it. Professor Pickering has made an emulsion containing 99 per cent of liquid petrolatum by shaking the oil, in successive portions, with a 1 per cent solution of sodium oleate. This is an oil-in-water emulsion, though only 1 per cent of it is water, and the proportion of soap in the finished emulsion is only 1 part in 10,000. A number of workers have experimented on soap emulsions, and while they do not agree exactly in the figures they all find that the most stable emulsions are obtained by using weak soap solutions,—usually under 1 per cent. When figured on an anhydrous soap, some recommend solutions of 0.15 to 0.50 per cent strength. Prepared soaps will always contain some water, even if powdered, and this will be allowed for in preparing such solutions. Cake soaps contain 20 to 36 per cent, and powdered soaps 1 to 10 per cent of water, as a rule. Soft soap contains 40 to 50 per cent.

Mr. Lenher and Miss Buell reported (Jour. Ind. and Eng. Chem., 1916) that in making 50 per cent emulsions with soap the following proportions were necessary:—

50 cc. oil of turpentine, 50 cc. water, 0.633 Gm. sodium oleate
50 cc. carbon tetrachloride, 50 cc. water, 0.114 Gm. sodium oleate
50 cc. chloroform, 50 cc. water, 0.782 Gm. sodium oleate
50 cc. benzol, 50 cc. water, 0.980 Gm. sodium oleate
50 cc. olive oil, 50 cc. water, 0.638 Gm. sodium oleate

These results show that different liquids need different amounts of soap, but that in all cases a 1 per cent solution of soap is sufficient for an emulsion containing half water. They also found that soap solutions emulsify more readily when warm, but if the soap is reduced the emulsions separate on cooling.

This all goes to show that soap is quite efficient as an emulsifying agent, and that only a small proportion is required. Pharmaceutically, soap emulsions are used only for preparations intended for external use, and the amount of soap needed will depend upon the proportion of emulsified body and the degree of dilution when it is used. Soap emulsions are best made by adding the oil, or other body, to the soap solution in portions, shaking after each addition. Intermittent shaking has been found to be more efficient than continuous, but as a rule the emulsion forms very quickly and but little shaking is needed.

Soap emulsions serve an excellent use in sprays, liniments, veterinary practice, etc. Soft soap and liniment of soft soap are convenient forms to use in making these mixtures. Alkalies will not emulsify volatile oils because these do not form soaps.

Linimentum Ammoniae and Linimentum Calcis are good illustrations of these mixtures or soaps, made directly from alkali. Liniment of soft soap is sometimes added surreptitiously to gum-emulsions to pre-

vent separating or to recombine oil already separated. If much has been added a frothing may be noticed when the emulsion is shaken.

Emulsions made with soap are incompatible with acids, which not only break the emulsions, but also decompose the soap.

Emulsions of copaiba are often ordered made with an alkali. This forms a smooth emulsion which stands well. The alkaline action is specially desired, and the emulsion is rendered more compatible with alcoholic bodies than when gum is used.

Woolfat is sometimes employed as an emulsifying agent for external preparations. It will emulsify a considerable proportion of a fixed oil, and it makes a very smooth emulsion. The woolfat should be melted and mixed with the oil, then warm water added gradually with constant agitation. These emulsions are easily made in a bottle, and can be diluted until quite thin without breaking.

Patent or secret emulsifiers are constantly appearing on the market. They appeal to the pharmacist because they are easy to use; the emulsifier and oil is put into the bottle, water is added, and a short agitation produces a white and creamy emulsion. They usually consist of soap or saponin with some gummy or albuminous body. Professor Arny has given the following, as a type of these emulsifiers. A mixture of 1 Gm. (15 grs.) of tragacanth, 0.65 Gm. (10 grs.) of saponin, and 0.015 Gm. (1/4 gr.) of saccharin forms the emulsifier. It is used in the proportion of 15 grs. to an ounce each of oil and water, the oil being placed in a dry bottle, the emulsifier added, then the water.

Such mixtures are attractive in the ease with which they accomplish results, but neither soap nor saponin is desirable for internal use.

Professor Arny recommends as the best "bottle-emulsifier," a mixture of equal parts of finely powdered gelatin, powdered tragacanth, and powdered sugar. Thirty grains of this is to be used for each ounce of oil. It requires a long shaking, but makes a white emulsion. It is essential that the gelatin be in fine powder.

Professor LaWall states that a mixture of 20 parts of powdered egg albumin and 80 parts of cream of tartar acts as an efficient emulsifying **agent for volatile oils**, in very small proportions. For the oils heavier than water such as oils of wintergreen, sassafras and clove, 1 Gm. of the agent is mixed with 100 cc. of the oil, then 100 cc. of water added and the whole shaken vigorously. For the lighter oils, 2.5 Gm. of the agent is needed for each 100 cc. of oil, the process being the same. This emulsifier makes very satisfactory emulsions with volatile oils and has the advantage that being itself acid it blends well with the flavor of the oil. It is not satisfactory for fixed oils, chloroform, benzol etc.

INSOLUBLE AGENTS

Finely divided solids, particularly freshly made and undried precipitates, can be used to make true emulsions which are as fine and permanent as those made with gums or albuminous agents.

Not all precipitates are efficient as emulsifying agents, but only such as are extremely fine and non-crystalline. The best of such are basic sulphates of iron (ferrous) or of copper, made by adding lime

water to a solution of ferrous sulphate or copper sulphate, one gram of copper sulphate requiring for this purpose 134 cc. of lime water. This will emulsify 4 to 6 cc. of oil, making an emulsion which will stand for months without separating. This has a technical value for spraying trees or shrubs, but is not likely to be ordered on prescriptions.

Milk of magnesia has been used as an emulsifying agent in pharmacy, and is very efficient. It does not act by reason of its alkalinity, but because of the fineness of the particles, which coat the oil globules and so prevent their coalescing.

Emulsions of heavy liquid petrolatum with milk of magnesia are now in common use. They are easily made by agitating the two together in a bottle or mortar. The electric mixer or an egg beater is especially satisfactory for making these. Milk of magnesia will be found to emulsify many other bodies with which it is sometimes combined, such as castor oil, tincture of jalap, etc.

Insoluble emulsifying agents have a considerable use in making emulsions for technical use. Some polishes or cleaners for automobiles, for instance, being an emulsion of liquid petrolatum with clay as the emulsifying agent. The clay must be of the colloid type and hydrated as fully as possible. One or two per cent of clay in the emulsion is sufficient to form a fairly stable emulsion. Emulsions of kerosene with basic copper sulphate for use as spray, etc. instance the technical uses of insoluble powders as emulsifying agents.

Dried, fine powders do not make as stable emulsions as fine—preferably colloidal—precipitates which are not dried. Milk of magnesia is therefore a better emulsifying agent than magnesium oxide. Most of the very fine precipitates which are undried will make emulsions, including freshly precipitated calcium carbonate, silica (water glass), calcium hydroxide, aluminum hydroxide, iron, zinc and lead hydroxides, calcium, iron and copper sulphates, the last two basic, metallic sulphides, etc. All of these will act as emulsifying agents in varying degrees, and the more colloidal the character of the precipitate the better the emulsifying action.

WATER-IN-OIL-EMULSIONS

Emulsions in which water is the internal or dispersed phase, and oil or a fat is the external or continuous phase, are usually not as stable as the oil-in-water type. There are some pharmaceutical preparations which come in this class but are not generally known as emulsions. Such are calamine and lime liniments—in which the water is emulsified by calcium oleate, the latter being formed by reaction of the solution of calcium hydroxide with the oil. Ointments containing water are technically emulsions of the water, and are made either with or without a special emulsifying agent, according to the proportion of water incorporated.

The emulsifying agents used for this type are either bodies which are soluble in oil or fats and are insoluble in water, or are bodies which are insoluble in either but are wetted easily by oil and not by water. The soluble agents are chiefly the oleates of the metals, the best of which for this purpose are the oleates of magnesium, calcium, and zinc.

But other oleates are also used. These are best adapted for making fluid emulsions.

Other agents which may be used for either fluid or semi-solid emulsions—and are more frequently used in ointments,—are **lecithin, cholesterol, woolfat, resin** and **beeswax**. The last three are particularly valuable in ointments, and are further treated under that subject.

Mercuric iodide is slightly soluble in oil, particularly when warm, and has been used to make a water-in-oil emulsion.

The insoluble agent best adapted is **soot** or **lampblack**. This is wetted by oil but repels water, so it makes a water-in-oil emulsion. Most insoluble emulsifying agents produce the other type.

This kind of emulsion can be diluted with oil, but repels water. Emulsions dilute according to their continuous phase:—the oil-in-water type dilute easily with water but break if much oil is added, and the water-in-oil type mix readily with oil or fats but take up only a very limited amount of water. This fact furnishes a means of distinguishing between the two types; the emulsion will dilute freely either with water or with oil according to which is the external phase.

Another method of distinguishing between them is to drop a very little of an oil-soluble dye on the surface. If it is an oil-in-water emulsion the dye will not spread, but if it is water-in-oil the color will spread over the surface.

The two types of emulsions will not mix with each other. They are antagonistic and will either invert or break each other. The reason for this is seen if we take an oil-in-water emulsion made with sodium oleate, and add to it a solution of calcium chloride. Interchange of the radicals will take place and we will have sodium chloride and calcium oleate formed, and the latter being insoluble in water cannot make an oil-in-water emulsion, but can make a water-in-oil emulsion. If the water is not in great excess the emulsion will first break, then invert to the other type.

If therefore we mix ammonia liniment with lime liniment we will find that according to the proportions mixed we may have (1) both emulsions broken and the oils separating, or (2) one emulsion broken and inverted, and the mixture converted into a single type emulsion. The two types of emulsions are incompatible with each other.

In making butter an inversion of the emulsion takes place. In the cream, the butter fat is emulsified by a proteid which is soluble in water, and an oil-in-water emulsion is the result. On churning this proteid is coagulated, then becomes insoluble in water and the butter fat coalesces and separates. But it has a small emulsifying power and so takes up some water and forms a water-in-oil emulsion.

Commercial paints contain a small amount of emulsified water which has an important action on their spreading and drying properties.

STABILIZING EMULSIONS

By stabilizing is here meant the means taken to keep the emulsion homogeneous,—*i.e.*: no separation into layers taking place.

There are three conditions which make for stability any one or two of which may apply in a given case. These are, (1) an optimum pro-

portion of oil and water, (2) the use of substances to increase viscosity, and (3) the employment of special apparatus to homogenize the emulsion.

In the first condition there is a certain **relation of oil to water** which is needed to form and to maintain an emulsion. Be it remembered that an emulsion, in the ordinary sense of the term, is a mixture of oil and water, and the presence of each is needed to make and hold an emulsion. Then if an emulsion consists of very small oil globules suspended in water, and prevented from coalescing by electrical conditions, and by a film of emulsifying material, there ought to be a certain ratio of the two in which they are in equilibrium, and neither is in excess.

Theoretically if spheres of uniform size are packed as closely as possible into a given space, they will occupy 74.048 per cent of the total volume of that space. Therefore if oil globules are uniform in size and are packed together as closely as possible there will be room between them for 25.952 per cent of the total volume which they occupy in water. In other words if we fill a vessel as completely as possible with small spheres, there will still be about a quarter of its capacity available for a liquid to fill the spaces between the spheres.

Therefore an emulsion which contains 74.048 per cent by volume of oil, and 25.952 per cent by volume of water should have the two in equilibrium and should show no separation into layers on standing. This has been found to be practically the case.

Professor Pickering proved the truth of this theory by preparing emulsions of liquid petrolatum in 1 per cent of soap solution, using different proportions of oil and water solution, and allowing them to stand twelve weeks, when the separation into layers was apparently complete. Samples of the top or cream layers were then analyzed and found to contain 77.7 per cent, 81 per cent and 81.9 per cent of oil respectively. These results are somewhat higher than the theoretical, which may be explained by the fact that the size of the globules in the emulsions are not entirely uniform, and also they are not all truly spherical. But the results are close enough to prove the soundness of this theory as applied to emulsions.

Practical experience also shows that an emulsion which contains from two thirds to three quarters of its volume of oil does not separate into layers even on long standing. Thus the primary emulsions made with powdered acacia and containing approximately two thirds of the total volume in oil, will not separate on standing. In this case viscosity also plays a part in hindering the separation. Emulsions containing an excess of oil tend to separate oil, and those containing an excess of water, separate water.

This also throws some light on why it is necessary to accurately measure the oil and the water in making the primary emulsion; the proportions are near to the theoretical equilibrium.

Viscosity regulation is the second method of securing stability. Since viscosity is a hindrance to motion, the more viscous the emulsion the less likely it is to separate into layers or to break.

Viscosity in an emulsion has a purely mechanical effect. It hinders flow, and flow being the cause of separation, either into layers or into oil and water, anything that increases viscosity decreases flow and so stabilizes, in some degree, the emulsion.

It is plain that there is a practical limit to making emulsions viscous for this purpose. We could make emulsions so viscous that they will not pour, and so prevent all separation. But that would not be acceptable when the emulsion is to be administered by the spoonful. Some ointments are emulsions, and do not separate, but we can not label them emulsions.

The thicker mucilages obtained from the use of tragacanth, Irish moss, agar, or starch, and the increased viscosity of solutions of sugar, honey, malt extract, licorice extract and glycerin are valued in emulsions for their viscosity more than for their own emulsifying powers. They frequently find their best purpose as adjuvants to emulsions in which other emulsifying agents are also used. Usually about 2 per cent of tragacanth is the easiest method to use at the prescription counter. But sugar, syrup, honey, glycerin and similar viscous bodies act similarly.

Homogenizing or Viscolizing.—Most commercial emulsions that are made in large quantities are finished in a homogenizing apparatus. This is a machine which subdivides the oil globules into smaller and more uniform sizes than can be secured in the usual emulsifying apparatus.

The smaller the globules of the emulsified oil, the more viscous and stable will be the emulsion. The nearer the globules are made to approach to the size of colloidal solutions, the more the emulsion will resemble a colloidal solution. In very weak emulsions, made without the use of an emulsifying agent, the oil globules are usually about the same size as the particles of metal in a colloidal solution. They exhibit the Brownian movement, and are practically colloidal solutions of oil in water. But such solutions contain not in excess of 2 per cent of oil. In pharmaceutical emulsions, containing 25 to 65 per cent of oil, the globules are larger. In milk the globules are variable in size, but usually average several times the size of colloidal particles in solution. When milk is run through the homogenizer the globules are reduced very much in size, and if the size is sufficiently diminished the milk will not separate a cream layer, and the cream will not churn into butter.

Homogenizers were originally designed for the treatment of milk which is distributed in bottles, to insure a uniform product in the different containers. The risk of getting individual bottles that, through failure to stir sufficiently, might fail to meet the legal requirements, are thus reduced.

The essential parts of the apparatus consists of a pressure pump by which the milk is forced through either very small orifices against a rapidly revolving plate, which by reason of its speed and the force of impact breaks the milk into a fine spray,—or the milk is forced between two conical surfaces, the distance between which can be regulated, and is small enough to break up the globules. The pressure required to force the milk through is usually from 2000 to 3000 lbs. per square inch, hence the space is very small.

Such machines are now adapted to the finishing of commercial emulsions, and are used by most manufacturers. The emulsion is made by churning in the usual manner, and is then transferred to the homogenizer. Since pharmaceutical emulsions are richer in oil than

milk, and also more viscous, the homogenizing valve is regulated for smaller pressures—usually 500 to 1500 lbs. per square inch. The globules are not then made as small as in homogenized milk, but the purpose of preventing separation is accomplished. Homogenizing (or viscolizing as it is sometimes called) increases the viscosity of the emulsion and thus prevents separation in two ways. The finer the globules in an emulsion, the more viscous will it be.

The Color of Emulsions.—Most emulsions are white or yellowish, and opaque. This is due to the different refraction of light which oil and water give, and also to the opaque solution or suspension of the emulsifying agent. If the solution of the agent is clear and the oil and water could be brought to the same refraction, the emulsion would be transparent. A patent has been taken out for making a transparent emulsion of cod liver oil by adding sufficient sugar to equalize the refractions. Glycerin has a similar effect on oil emulsions. But it is difficult to get a transparent emulsion of an oil which will contain a considerable proportion of the oil.

Professor Holmes has found that an emulsion of amyl acetate in glycerin, made by means of pyroxylin as the emulsifying agent, can be made to change in color and transparency by the addition of carbon disulphide.

The addition of a solution of potassium iodide to an emulsion of liquid petrolatum with sodium oleate solution is said to result in a varying display of colors. These are interesting phenomena, but are of much less importance than the therapeutic effect and flavor of emulsions.

GENERAL SUGGESTIONS

Remember that water is as necessary as oil to form an emulsion, and the way it is used determines the success of the emulsion.

It is sometimes difficult to give up the notion that "oil and water will not mix," and to appreciate that in an emulsion we have overcome a law of repulsion, but an emulsion is a triumph of skill, a combining of bodies which are naturally repellent.

This is accomplished, not by brute force or energy, but by judgment and skill in combining them. Emulsions are *coaxed* into being, not forced. The oil and water need a third body to get them to combine, to introduce them to each other, so to speak. What tact is to society, the emulsifying agent is to the emulsion. It introduces the antagonistic bodies, overcomes their antipathies, brings them into intimate contact, and holds them together in harmony.

For general pharmaceutical use, acacia is the best agent. More emulsions are made with it than with all other agents together. A large proportion of the commercial emulsions that are used in pharmacy and medicine are made with acacia as the chief emulsifying agent.

Powdered acacia is easier and more certain in use than is mucilage of acacia. It serves a double purpose in forming the emulsion. First by mechanical action, before it dissolves, it aids in subdividing the oil. Then as it goes into solution in the water it coats the globules with a film of mucilage and prevents their coalescence. It is first

mixed with the oil in a *dry* mortar because powdered acacia, in common with many fine powders, occludes much air and does not allow water to penetrate it easily. Oil diffuses it, allows the air to escape, and then when the water is added it dissolves promptly instead of matting together. It is not advisable to allow it to stand in contact with the oil for a very long time because it seems to be slightly, though slowly, soluble in oil and then tends to make the water-in-oil type of emulsion. This interferes with its regular function as a water-soluble agent and the emulsion may refuse to form. Tragacanth, which is commonly combined with acacia to impart viscosity to the emulsion and thus prevent separation into layers, acts similarly. It is difficult to get a prompt solution of these powdered gums if water is added directly, but if the air is first displaced and the gums dispersed in a little oil or alcohol, the gum dissolves very quickly when water is added.

Acacia produces its best effect in emulsions of the fixed and volatile oils. It makes a good emulsion with liquid petrolatum, but does not emulsify this as easily as it does the glycerides. Gelatin, agar and egg albumin, which are not very satisfactory for the fixed and volatile oils, emulsify liquid petrolatum quite readily, and make white emulsions. These agents are changed in character by prolonged agitation,—the gelatin being liquefied and the albumin coagulated,—and it is thus easier to break the emulsion by too much agitation when these are used.

Extract of malt is preferred for cod liver oil emulsions because both by its taste and viscosity it covers the fishy taste of the oil. It is usually employed in excess of the oil in emulsions. Emulsification with extract of malt is facilitated by a little heat,—enough to soften the extract and make the agitation or trituration easier. A warm mortar is an aid in this case.

Yolk of egg is another of the more common pharmaceutical emulsants. It has **two special advantages**. It is easy of operation, produces palatable emulsions, and is effective in acid emulsions. Most of the pharmaceutical emulsifying agents give their best results in emulsions which are approximately neutral. They are apt to break if the emulsion is made very acid or strongly alkaline. Yolk of egg will stand considerable acid in the emulsion without breaking, and is preferred in the decidedly acid combinations.

The thickening agents,—tragacanth, Irish moss, starch, etc. need to be used with judgment. In the absence of a homogenizer they are almost necessary for emulsions which are to be kept in stock, but if used too freely the emulsion may become too thick to pour, and the tendency to separate into layers is not diminished in proportion to the thickness. An emulsion which has about the same viscosity as glycerin or syrup is sufficiently thick for all purposes.

Emulsions of vegetable oils or of cod liver oil are apt to darken at the top on long standing. This is due to oxidation. Manufacturers prevent this by displacing the air in the bottle by an inert gas,—carbon dioxide or nitrogen. This also prevents, in a measure, fermentation of the emulsifying agent or syrup with which it is flavored.

Some preservative is needed in emulsions which are to be stored to prevent putrefaction processes on albuminous agents and fermentative processes or gums and saccharine bodies. The best preservative for

the purpose is alcohol, in the proportion of 7 to 12 per cent. Benzoic acid is sometimes used, but is less effective. Unless the emulsion is particularly sensitive to change, or is likely to be kept for some time, no preservative is needed.

The agitation in making an emulsion should be brisk but not violent. Curiously enough a slow shaking may break an emulsion when a rapid agitation would restore or make it. The time necessary to agitate is not uniform with different oils and agents, but usually is short. In making a primary emulsion with acacia, the emulsion usually forms within one minute after agitation is begun.

If it does not come within two or three minutes something is wrong, though a longer agitation may get it.

In making emulsions by agitation in a bottle, it has been found that intermittent agitation produces results more rapidly than continuous. Thus if the bottle be agitated well for 15 or 20 seconds, then allowed to rest for one or two minutes, the agitation and rest then repeated a few times, a better emulsion will be formed than if the agitation is continuous for several minutes. The reason for this is not clear, and it is not known to apply to emulsions made in a mortar or emulsifying apparatus. But the agitation should be brisk in any case. The greater the proportion of oil, the longer the agitation is needed.

Emulsions of volatile oils are improved by mixing them with an equal or double volume of a fixed oil, before emulsifying. The fixed oil thickens the emulsion and makes it more creamy. For instance an emulsion of turpentine is best made by first mixing it with twice its volume of expressed almond oil, then emulsifying the mixture with powdered acacia. The quantity of acacia to use must be calculated on both the volatile and fixed oil basis, using half acacia for the volatile oil and one fourth for the fixed; then twice as much water as acacia.

Resinous tinctures will emulsify when poured into water if the pouring is slow and the agitation rapid. The best method is to place the aqueous liquid in a graduate or beaker, pour the tincture into the center of the liquid in as small a stream as possible, and stir the liquid rapidly with a glass rod or other suitable implement. The tincture should not be allowed to flow down the sides of the container, and must be diffused through the liquid as rapidly as possible. As in an emulsion of oil, the finer the precipitate of resin the better it will remain diffused.

When the resinous matter is in too large proportion to remain diffused without the aid of an emulsifying agent, honey, extract of malt, or tragacanth are good suspending agents to use.

One ounce of tincture of benzoin to a pint of mixture is about the limit when no emulsifying agent is used, unless an alkali is added. Emulsions intended for external use should not be made with gums or any agent that will dry to a sticky or hard condition. Some of the liniments illustrate this point. The emulsifying agents most used for liniments are soap and white of egg. Occasionally preparations are desired for application to the hair or to the skin which are not liniments or lotions but which contain some oily, waxy or resinous ingredients that need to be emulsified in order to make a presentable preparation. A very small amount of soap,—liniment of green soap is very convenient—offers the best agent as a rule. Only enough soap

to make the emulsion should be used—perhaps 0.25 to 0.5 per cent. Tincture of quillaja may also be used. This is not very satisfactory when the proportion of oil is large, but gives good results with small amounts.

Solid organic compounds, such as salol, iodoform, aristol, sulphonal, trional etc., when ordered in liquid mixtures, may be dissolved in a fixed oil, which is then emulsified. They act more promptly when administered in this way. Salol is very soluble in almond oil, but the others are less soluble and should be dissolved in a warm oil to save time. Aristol, iodoform and trional require about 20 parts of warm oil, and sulphonal 40 parts. The use of oil solutions of compounds which are insoluble in water is increasing.

Flavors are needed to make emulsions palatable and need judgment in the using. The National Formulary gives a number of aromatic mixtures which can be employed with good effects. The aromatic and pungent flavors do not disguise an oil as well as softer flavors. For cod-liver oil, malt extract or licorice extract, with just a trace of clove or mint, are the most effective disguises. Coffee is largely used in Europe in cod-liver oil emulsions. Vanilla, chocolate, and tolu are also excellent, particularly the last two.

Mr. Geo. M. Beringer, Jr. reported on a series of experiments undertaken to classify the various flavors suitable for emulsions of cod-liver oil, that oils of coriander, geranium, cardamom, and anise most successfully concealed the fishy odor and taste of the oil. A second group consisting of oils of bitter almond, clove, and pimento and also vanillin, partly covered the odor and taste of the oil, but were very persistent and of most value in blending with other flavors. Oils of peppermint, spearmint, lemon, orange and Ceylon cinnamon he found to mask the odor but not the fishy taste of the oil. And oils of caraway, cassia, sassafras, wintergreen and nutmeg he found to actually accentuate the fishy taste. Coumarin and cocoa he did not find satisfactory.

A little salt aids in covering the fishy taste of cod-liver oil, and sugar should be used sparingly. Marked sweetness does not blend well with the oil and may easily spoil the effect of an otherwise good flavor.

All flavors need sweetening to make them palatable. Syrup or sugar is best, and should be added to the emulsion after everything else is in. Sugar is not friendly to emulsions, and if used too freely it may break the emulsion. Saccharin, in the proportion of a quarter of a grain to an ounce of oil, is recommended. Sometimes a combination of sugar and saccharin is to be preferred.

EMULSIONS

I

- R. Ammoniac..... 40 Gm.
 Water, a sufficient quantity to make..... 1000 cc.
 M. Sig.—Emulsion of ammoniac.

Rub the ammoniac in a warmed mortar, with 900 cc. of water, at first very gradually added until a uniform emulsion results. Then strain the mixture into a graduated vessel, and wash the mortar and strainer with enough water to make the product measure 1000 cc. Make four fluidounces.

- 2
- R. Sweet almond..... 60 Gm.
 Acacia, in fine powder . 10 Gm.
 Sugar..... 30 Gm.
 Water, a sufficient quantity to make..... 1000 cc.
- M. Sig.—Milk of almond.

Having blanched the almond, add the acacia and sugar, and beat them in a mortar, until they are thoroughly mixed. Then rub the mass with 900 cc. of water, at first very gradually added, until a uniform mixture results. Strain this into a graduated vessel and wash the mortar and strainer with enough water to make the product measure 1000 cc. Mix the whole thoroughly.

Make four fluidounces. Blanch the almond by soaking in warm water until the skins are loosened.

- 3
- R. Amygdalæ dulcis..... 20.00
 Olei ricini..... 30.00
 Sacchari..... 15.00
 Aquæ..... q. s. ut. ft. 100.00
- M. Ft. haustus. Sig.—Summatur statim.

- 4
- R. Olei morrhuae..... 50
 Pulv. acaciæ..... 8
 Pulv. tragacanthæ..... 2
 Aquæ..... ad. 100
- M. Ft. emuls.

Mix the acacia and tragacanth with the oil, add 40 cc. of water and triturate until emulsified, then add water to make 100 cc.

- 5
- R. Hydrarg. bichlorid..... gr. iv
 Acid hydrochloric..... 5 j
 Amygdal. amaræ..... 3 iv
 Glycerin..... 3 iij
 Tinct. benzoini..... ℥ xv
 Aquæ amygdal. amaræ.... 3 iv
- M. s. a. Sig.—"Freckle lotion."

Blanch the almond and beat into a paste with the glycerin, to which gradually add 3iij of the water. Place in a bottle and add the tincture of benzoin in very small proportions, constantly agitating. Lastly add the remainder of the water, in which the corrosive chloride and the acid have been dissolved.

- 6
- R. Olei morrhuae..... 3 j
 Mucilaginis chondri (N. F.). 3 v
 Aquæ..... 3 iij
- M. Sig.—"Carrageen mixture."

Place the mucilage in a pint mortar and triturate with the oil, added very slowly and in portions, taking care that each portion is well emulsified before adding the next. Lastly, add the water.

- 7
- R. Acaciæ pulveris..... 10
 Sacchari pulveris..... 30
 Olei morrhuae..... 60
 Aquæ..... ad. 120
- M. Fac. emulsionem. Sig.—Capiat 3j pro doso.

(a) Make a primary emulsion with the acacia, 40 cc. of oil and 15 cc. of water, add the remainder of the oil in portions, alternating with portions of water, and lastly add the sugar dissolved in the remainder of the water.

(b) Make a mucilage with the acacia and 20 cc. of water; in this dissolve the sugar, and then add 40 cc. of oil in portions, thoroughly emulsifying each portion before the next is added. Then add the rest of the oil alternately with water.

- 8
 R. Olei jecoris aselli..... 32
 Olei gaultheriæ..... 0.30
 Fiat emulsionis..... 64
 M. Sig.—"Acacia emulsion."
- 9
 R. Olei jecoris aselli..... 30.0
 Mucilaginis acaciæ..... 15.0
 Olei gaultheriæ..... 0.5
 Aquæ menthæ viridis..... 15.0
 M. Sig.—8 cc.
- 10
 R. Olei morrhuæ..... ʒ j
 Glyceriti vitellæ..... ʒ ijss
 Aquæ.....ad. ʒ ij
 M. Sig.—"Glyconin mixture."
- 11
 R. Olei morrhuæ..... ʒ iv
 Ovi vitellæ..... ʒ iii
 Glycerini..... ʒ ii
 Acidi phosphor. dil..... ℥ xl
 Spir. vini gallici..... ʒ i
 Olei amygdal. amar..... ℥ vi
 Aquæ aurant. flor.....ad. ʒ iv
 M. Ft. emuls.
 Sig.—Phosphatic emulsion.
- 12
 R. Olei terebinthinæ..... 8.0
 Pulv. tragacanthæ..... 1.0
 Syrupi..... 15.0
 Aquæ.....q. s. ut. ft. 60.0
 M. Ft. emulsio.
- 13
 R. Olei lini..... ʒ vij
 Tinct. quillajæ..... ʒ ss
 Syrupi..... ʒ j
 M. Sig.—85 per cent emulsion.
- 14
 R. Olei morrhuæ..... ʒ j
 Dextrini..... ʒ ii
 Aquæ.....ad. ʒ ii
 M. Sig.—"Dextrin emulsion."
- 15
 R. Olei morrhuæ..... ʒ ij
 Ext. glycyrrhizæ pulv... ʒ ss
 Confect. amygdal..... gr. xij
 Spt. lavand. comp..... ʒ j
 Spt. menth. pip..... ℥ xxxv
 Syr. tolut..... ʒ vij
 M. Sig.—Black mixture.
- Make according to the rule for emulsions, using 8 Gm. of powdered acacia. Also make using 4 Gm. of powdered acacia.
- Place the mucilage in a mortar and gradually add 20 cc. of cod-liver oil, triturating thoroughly after each addition. Then add the remainder of the oil in portions of 2 to 3 cc., alternating with 1 to 1 1/2 cc. of spearmint water; lastly add the oil of wintergreen and the remainder of the spearmint water.
- Add the oil gradually to the glycerite, with constant stirring; lastly, add the water.
- Mix the yolk of egg and glycerin and add the cod-liver oil. Triturate until emulsified, then add the other ingredients in order.
- Place the oil in a dry bottle, add the tragacanth, shake, add 15 cc. of water and shake vigorously until an emulsion results. Add the remaining ingredients gradually.
- Place the tincture in a dry bottle, gradually add the oil, and emulsify; lastly, add the syrup.
- Make in same way as carrageen emulsion. (See. No. 6)
- Triturate together the extract of licorice and confection of almond, mix well with the syrup of tolu, and add to this slowly the cod-liver oil with constant trituration. When all is emulsified add the spirits in portions. This forms a dense, black, permanent emulsion, in which the taste of the cod-liver oil is quite effectually masked.
- (The confection of almond is made by mixing 6 Gm. blanched almond, 1 Gm. of powdered acacia and 3 Gm. of sugar.)

16

- R. Tragacanthæ pulv. 3 j
 Acaciæ pulv. 3 iss
 Marantæ. 3 j
 Olei morrhuæ. 3 vj
 Aquæ. 3 vj
 Spiritus chloroformi. 5 j
 Saccharini. gr. iij
 Olei cinnamomi. m ix
- M. Fac. emulsionem.
 Sig.—Ut dictum.

Put the powders in a dry mortar, rub to a smooth paste with a little oil, add the remainder of the oil, mix well, then add all of the water and triturate quickly until emulsified.

Dissolve the saccharin and oil of cinnamon in the spirit and incorporate.

17

- R. Olei morrhuæ. 3 iv
 Syr. pruni virgin. 3 ij
 Extracti malti. 3 j
 Vini xerici. 3 j
- M. Ft. emuls.
 Sig.—Malt emulsion.

Emulsify the oil by gradual addition to the extract of malt, in a warm mortar, alternating with the syrup. Lastly add the wine.

18

- R. Spiritus camphoræ. 5 ij
 Spiritus chloroformi,
 Tinct. lavand. comp. aa 5 j
 Mucil. tragacanth. 5 j
 Aquæ. 3 iij
- M. Sig.—Sedative mixture.

19

- R. Olei ricini. 3 j
 Acaciæ pulv. 3 ij
 Olei amygdalæ amaræ. m ij
 Olei caryophylli. m j
 Liquoris saccharini. m iv
 Aquæ. ad. 3 iv
- M. s. a. Sig.—Pro alvo.

20

- R. Acaciæ pulveris,
 Tragacanthæ pulv.,
 Marantæ. aa 3 ss
 Pepsini saccharati. 3 j
 Olei morrhuæ. 3 iv
 Olei cinnamomi. m iv
 Olei sassafras. m iij
 Olei amygdalæ amar. m j
 Olei gaultheriæ. m iij
 Glycerini. 3 iv
 Syr. hypophosph. cum ferro 3 v
 Acid phosphorici dilut. 3 iij
 Aquæ destillatæ. ad. 3 viij
- M. Fac. emulsionem.
 Sig.—“Phosphatic emulsion.”

Mix the gums, arrowroot and pepsin with 3i of oil, add 3vi of water and emulsify thoroughly, then add alternately the remainder of the oils and the water. Lastly, add the syrup and the acid previously mixed with the glycerin.

21

- R. Olei morrhuæ. 30.0
 Mucil. chondri. 15.0
 Aquæ amygdal. amar. 15.0
- M. Signa.—Tablespoonful.

Use the official mucilage of Irish moss for this.

22

- R. Cera albæ,
 Cetacei,
 Saponis pulveris,
 Sodii boratis. aa 1.0
 Amygdalæ dulcis. 15.0
 Alcoholis. 15.0
 Aquæ amygdalæ amaræ. 60.0
- Misce et cola. s. a. Sig.—“Toilet cream.”

Blanch the almond by soaking in warm water (about 40° C.), for half an hour, and after removing the skins bruise in a large mortar and rub to a smooth paste with 20 cc. of bitter almond water, then dilute with 20 cc. or more of the water.

Melt the wax and the spermaceti and mix with the soap and borax in a small warm mortar, and gradually add 20 cc. of warm bitter almond water. When cold mix the two emulsions, and add the alcohol. Strain through cheese-cloth.

23

- R. Terebinthinæ Canadensis ʒ ij
 Chloroformi..... ℥ xx
 Tinct. opii deodorat..... ʒ ij
 Spiritus gaultheriæ..... ʒ j
 Syrupi senegæ..... ʒ j
 Syrupi tolu..... ʒ xviii
 M. s. a. Sig.—A teaspoonful every
 2 hours.

Weigh the Canada balsam into a bottle containing the chloroform and spirit, shake until the balsam is dissolved, then add the syrup of senega and shake vigorously until a smooth emulsion is formed. Then add the syrup of tolu in portions, and lastly the tincture.

24

- R. Olei morrhuæ..... ʒ iij
 Liq. pancreatini..... ʒ iv
 Mucilaginis acaciæ..... ʒ iv
 Olei gaultheriæ..... ℥ xv
 Syr. calcii lactophosph..... ʒ j
 M. Ft. emulsio.
 Sig.—"Pancreatic emulsion."

Mix the pancreatin solution with the mucilage, add the oils gradually, and emulsify, and lastly, add ʒi of simple syrup, in which 15 grains of commercial calcium lactophosphate have been dissolved.

(The official syrup of calcium lactophosphate contains free acid, which is incompatible with the bicarbonate in the pancreatin solution.)

25

- R. Misturæ olei terebinthinæ... 60.0
 (Each cl. to contain i cc. oil turpt.)
 M. Sig.—i 1/2 cl. ante edente.

Use acacia in proportion to 0.5 Gm. to each cc. of oil.

26

- R. Ol. terebinthinæ..... ʒ jss
 Ovi recentis..... no. j
 Olei limonis..... ʒ ss
 Acid aceticæ..... ʒ iiss
 Aquæ..... ad. ʒ ivs
 M. Sig.—"Stokes' liniment." *Shake.*

Triturate the egg and oils together in a mortar until they are thoroughly mixed, then incorporate the acid and water.

27

- R. Chloroform..... 40 cc.
 Expressed oil of almond. 60 cc.
 Tragacanth, in very fine
 powder..... 15 Gm.
 Water, a sufficient quan-
 tity to make..... 1000 cc.
 M. Sig.—Chloroform emulsion.

Introduce the tragacanth into a perfectly dry bottle of sufficient capacity, add the chloroform, and shake the bottle thoroughly, so that every part of the surface may become wetted. Then add about 250 cc. of water, and incorporate it by vigorous shaking. Next add the expressed oil of almond, in several portions, shaking after each addition, and when the oil has been thoroughly emulsified, add enough water, in divided portions, shaking after each addition, until the product measures 1000 cc.

Make four fluidounces.

28

- R. Bromoformi..... ʒ ss
 Tinct. tolu..... ʒ j
 Mucil. acaciæ..... ʒ ij
 Syrupi..... ʒ iv
 Aquæ menthæ viridis... ad. ʒ ij
 M. s. a. Sig.—"Bromoform mixture."

Place the mucilage and two drachms of syrup in a bottle, and *gradually* add, with vigorous shaking, the bromoform and tincture of tolu previously mixed. When completely emulsified, add the remainder of the syrup and the spearmint water, with constant shaking.

29

- R. Pulv. acaciæ..... ʒ j
 Olei lini..... ʒ xv
 Olei cinnamomi..... gtt. viij
 Olei gaultheriæ..... gtt. xv
 Glycerini..... ʒ vi
 Syrupi..... ʒ x
 Spiritus frumenti..... ʒ ij
 Acid hydrocyan. dil..... gtt. x
 Chloroformi..... ʒ v
 M. Sig.—Compound linseed emulsion.

31

- R. Petrolati..... 22.5
 Olei amygdal. exp..... 22.5
 Acaciæ pulv..... 12.5
 Tragacanthæ pulv..... 2
 Aquæ..... ad. 100
 M. Ft. emuls.

- R. Emulsionis terebinthinæ Can-
 adenis 2 per cent..... 100.0
 Sig.—“Fir balsam emulsion.”

- R. Copaibæ..... 4.0
 Mucilag. acaciæ..... 6.0
 Olei gaultheriæ..... 0.250
 Tinct. lavand. comp..... 4.0
 Aquæ destillatæ..... 45.0
 M. Sig.—ʒ ij t. i. d. post edente.
 Compound by two methods.

- R. Copaibæ..... 8.0
 Liquoris potassæ..... 2.0
 Olei gaultheriæ..... 0.186
 Glycerini..... 15.0
 Aquæ cinnamomi q. s. ut. ft. 60.0
 M. Sig.—4 p. r. n.

36

- R. Olei morrhuæ..... ʒ ij
 Ovi vitelli..... ʒ j
 Sodii chloridi..... gr. xij
 Liq. saccharini..... ℥ iij
 Olei caryophylli..... ℥ iij
 Aquæ..... ad. ʒ iv
 M. F. emulsio.

10

30

- R. Ovorum..... no. iv
 Sodii chloridi..... gr. iv
 Glucosi syr..... ʒ ij
 Mucilag. amyli..... ʒ iv
 Lactis..... ʒ iv
 M. Ft. enema. Sig.—Nutrient
 enema.

32

- R. Terebeni,
 Ol. gossyp. sem..... aa ℥ clx
 Pulv. acaciæ..... ʒ vj
 Pulv. sacchari..... ʒ ij
 Aquæ..... q. s. ut. fiat. ʒ iv
 M. Ft. emulsio. Sig.—“Terebene
 emulsion.”

33

This can be made with acacia (2 Gm.), mucilage of acacia (6 cc.), tragacanth (0.5 Gm.), glyconin (8 cc.), or any of the other emulsifying agents.

“Chian” and other hard turpentine or balsams must first be dissolved in an equal or double volume of ether, and this mixture emulsified in the usual manner.

34

(a) Place the mucilage in the bottle, flow around the sides, add the copaiba and oil, shake well, add 5 cc. of water, shake and gradually add the remainder of the water and lastly the tincture, shaking after each addition. Label “Bottle method.”

(b) Place the mucilage in a mortar, add the oil, then the copaiba in portions, triturating actively, then the water gradually and lastly the tincture. Label “Mortar method.”

35

Place the solution of potassa, with 4 cc. of cinnamon water, in a 60 cc. bottle, add the copaiba gradually, shaking well, then the oil, glycerin and balance of the cinnamon water in order.

37

- R. Ammonia water..... 25 cc.
 Sesame oil..... 75 cc.
 Mix.—“Volatile Liniment.”

38

- R. Creosoti..... 2.0
 Lactis concentrat..... 20.0
 Ol. cinnamomi..... 0.65
 Aquæ.....ad. 100.0
 M. Ft. emulsio. Sig.—“Creosote emulsion.”

Triturate the condensed milk with an equal bulk of water, add the creosote and oil, triturate thoroughly, and incorporate the water gradually.

39

- R. Terebeni..... m. clx
 Acaciæ pulv..... gr. cl
 Ol. menth. pip..... m. xx
 Ext. glycyrrhizæ fld..... 3 j
 Glycerini..... 3 ij
 Aquæ.....ad. 3 ij
 M. Ft. emuls. Sig.—Terebene emulsion.

Mix the terebene, oil and acacia in a dry mortar, add 180 minims of water and stir until the emulsion forms.

Add the glycerin and the remainder of the water gradually, and lastly, the fluid extract of licorice. (C. E. Dotey, Ph. G.)

40

- R. Paraldehydi..... 3 viij
 Ovi vitelli..... no. vj
 Olei cassiæ..... 3 ss
 Sacchari pulv..... 3 j
 Aquam.....q. s. ad. 3 xvj
 M. Sig.—Paraldehyde emulsion.

- R. Solution of lime.
 Linseed oil, of each, one volume.
 Mix them by agitation.
 Sig.—Carron oil.
 Make two fluidounces.

41

42

- R. Paraffini duri..... 22
 Sevi..... 3
 Sapo mollis..... 2
 Tragacanthæ..... 2
 Glycerini..... 12
 Olei lavandulæ..... 1
 Aquæ bullientis..... 68
 M. Ft. emuls.
 Sig.—“Shaving cream.”

Melt the paraffin and suet in a bottle, add the boiling water in which the soap has been dissolved, and shake vigorously until a smooth emulsion has been formed. To this add the tragacanth in portions, keeping the mixture hot. Lastly, add the glycerin and oil, and shake while cooling.

43

- R. Olei ricini,
 Aquæ ammoniæ,
 Ammonii carbonat.....aa 3 j
 Alcoholis..... 3 iv
 Aquæ.....q. s. ut. ft. 3 viij
 M. s. a.
 Sig.—“Volatile Shampoo.”

44

- R. Whale oil soap..... 1 oz.
 Kerosene oil..... 2 pints
 Boiling water..... 1 pint
 Mix. Label “Kerosene insecticide.”

Dissolve the soap in the boiling water, add the kerosene, and churn them together by means of a large force syringe until completely emulsified.

(This is a standard insecticide. It is diluted with 3 to 10 parts of water and sprayed upon trees or shrubbery.)

45

- R. Zinci chloridi..... gr. iij
 Iodoformi..... gr. jss
 Acid salicylici..... gr. ij
 Adipis lanæ..... 3 ij
 Olei amygdal. exp..... 3 iss
 Aquæ.....ad. 3 iij
 M. Sig.—Injection.

Triturate the wool fat with the oil, gradually added; dissolve or suspend the solids in the water, previously heated, and stir into the oily mixture in portions. A smooth, viscid emulsion results. This can also be made in a bottle.

46

- R. Olei terebinth..... 3 iv
 Olei olivæ..... 3 ii
 Saponis..... 3 i
 Sodii chloridi..... 3 iv
 Aquæ ferventis..... 0 j
 M. Ft. enema.

Dissolve the soap in the warm water, mix the oils, and shake with the soap solution until thoroughly mixed.

47

- R. Camphoræ..... 1.00
 Pulveris acaciæ..... 2.00
 Decoctionis lini..... 250.00
 Ovi vitelli..... no. j
 M. Ft. enema. Sig.—Inject as directed.

Powder the camphor finely, add the acacia and yolk of egg, mix well and stir in the decoction of flaxseed gradually.

48

- R. Camphoræ..... 0.5
 Acaciæ..... q. s.
 Aq. destillatæ..... 100
 Syr. althææ..... 20
 M. Ft. emulsio.

Use 2.5 of camphor liniment, and emulsify with an equal weight of acacia.

49

- R. Camphoræ..... 1.0
 Tragacanthæ..... 1.0
 Syrupi..... 10.0
 Aquæ..... 50.0
 M. Ft. emulsio.

50

- R. Salol..... 10.0
 Acaciæ pulv..... 5.0
 Aquæ..... ad. 50.0
 M. Ft. emuls. Sig.—Salol emulsion.

Dissolve the salol in 20 cc. of olive oil, add the acacia and 10 cc. of water and triturate until emulsified. Lastly, add the rest of the water.

51

- R. Salol..... 3 j
 Pulv. acaciæ..... 3 j
 Pulv. tragacanthæ..... gr. x
 Tinct. tolu..... 3 ijss
 Syrupi tolu..... 3 j
 Aquæ..... ad. 3 iiij
 M. Sig.—"Salol emulsion."

Dissolve the salol in 3ij of oil and emulsify.

52

- R. Trional..... 1.00
 Olei amygdalæ exp..... 20.00
 Acaciæ..... 4.00
 Sacchari..... 8.00
 Aquæ aurantii flor..... 15.00
 Aquæ amygdal. amar..... 10.00
 Aquam..... ad. 60.00
 M. Ft. emuls.

53

- R. Potassii chloratis..... 3 j
 Tinct. cinchonæ comp..... 3 iii
 Tinct. guaiaci ammon..... 3 iii
 Ol. menth. pip..... m xv
 Mellis..... 3 vi
 Aquæ..... ad. 3 iv
 M. s. a. Sig.—Gargle.

Mix the tinctures, oil and honey, agitating thoroughly. Dissolve the chlorate in the water and add, gradually, to the honey mixture.

- 54
- R. Calaminæ..... ʒ ij
Zinci oxidi..... ʒ ij
Olei olivæ..... ʒ iv
Sulphur præcip..... ʒ ss
Acidi carbolici..... ʒ iii
Aquæ..... ad. 0 j
- M. Mix the powders with ʒiv of water, add the oil and heat gently until the latter is saponified, stirring constantly. Then add the rest of the water, and lastly the carbolic acid.
- 55
- R. Resinæ guaiaci..... gr. xxiv
Acaciæ pulveris..... gr. xij
Sacchari..... gr. xxiv
Aquæ cinnamomi..... ʒ ij
- M. Sig.—“Guaiac mixture.” *Shake.*
- 56
- R. Sodii boratis..... gr. xxv
Saponis pulv..... gr. xv
Olei theobromatis..... ʒ ij
Olei cocois..... ℥ xv
Aquæ rosæ..... ad. ʒ v
- M. Sig.—Cocoa Milk.
- 57
- R. Quininæ et urea chlorid..... 0.6
Hydrargyri salicylatis..... 3.0
Adipis lanæ..... 1.0
Olei olivæ..... 30.0
- M. Sig.—For injection
- 58
- R. Pilocarpinæ chlorid..... gr. vi
Tinct. pilocarpi..... ʒ iv
Spiritus rosmarini..... ʒ ii
Petrolati liquidi
Alcoholis..... āā ʒ iv
- M. Sig.—For scalp treatment. Use externally.
- 59
- R. Liq. plumbi subac..... ʒ ii
Glycerini..... ʒ ii
Phenolis..... āā ʒ ii
Olei. olivæ..... ʒ ix
- M. Sig.—For external use.
- 60
- R. Sodii salicylatis..... ʒ iii
Potass. bicarb..... ʒ i
Tr. guaiaci ammon..... ʒ iv
Emuls. petrolei..... ʒ ii
Aq. chloroformi..... ad. ʒ viii
- M. Dissolve the sodium salicylate in ʒiii of chloroform water and gradually add the tinct. guaiac. (The sodium salicylate solution dissolves the guaiac resin.) Then mix with the emulsion and finally add the rest of the chloroform water in which the bicarbonate has been dissolved.
- 61
- R. Santonini..... gr. i
Olei ricini..... ʒ iii
Olei menthæ pip..... ℥ vi
Mucilaginis acaciæ..... ad. ʒ iss
- M. Ft. emuls. Sig.—One tablespoonful at night.

62

Kerosene Emulsion

R.	Lime.....	2.2 Gm.	Slake the lime, mix with the water
	Kerosene.....	11.0 cc.	and add the kerosene. Shake or churn
	Water.....	88.0 cc.	vigorously until emulsified
	Make an emulsion.		

63

Bordeaux Emulsion

	Lime.....	0.3 Gm.	Slake the lime and add 60 cc. of
	Copper sulphate.....	1.6 Gm.	water. Dissolve the copper sulphate
	Liquid petrolatum.....	6.0 cc.	in 30 cc. of water and add to the lime
	Water to make.....	100.0 cc.	solution. Then add the liquid petro-
			latum and shake or churn until
			emulsified.

64

R.	Ichthyoli.....	℥ ij	Makes a smooth emulsion by any
	Olei olivæ.....	℥ j	order of mixing.
	Liq. plumbi subacet.....	℥ j	

M.

65

R.	Camphoræ.....	0.2	Dissolve the camphor and menthol in
	Mentholis.....	0.3	the oil, add to the milk of magnesia
	Ol. pini pumil.....	2.0	and mix thoroughly. (Lascoff.)
	Magmæ magnesiae.....	60.0	

M. Sig.—As directed.

66

R.	Tinct. benzoini co.....	℥ i	Rub the compound tincture of
	Eucalyptolis.....	℥	benzoin with 15 grs. lanolin and
	Benzoinolis liq.....	ad. ℥ i	gradually add the benzoinol, then the
M.	Ft. nebula.		eucalyptol. A little heat aids in
	Sig.—Use as spray on the throat.		securing a smooth mixture. (Lascoff.)

67

R.	Ol. ricini.....	℥ iss	Dissolve the menthol and oil of
	Tr. opii camph.....	℥ vi	wintergreen in the castor oil, add 4
	Pulv. acaciæ.....	q. s.	drachms of powdered acacia, mix well
	Syr. pruni virg.....	℥ ii	then add 1 1/2 oz. of Brown mixture and
	Tr. gentianæ co.....	℥ ii	make an emulsion. To this add first
	Menthol.....	gr. iv	the syrup of wild cherry, then the
	Ol. gaultheriæ.....	℥ iv	tinctures, then the citric acid and
	Acid citric.....	gr. v	enough Brown mixture to make 6 ounces.
	Mist. glycyrrhiz co. ad.	℥ vi	

M.

68

R.	Olei morrhuae.....	℥ i	Emulsify the oil first with 4 oz. lime
	Syr. ferri iodidi.....	℥ vi	water, then add the other ingredients.
	Tr. gaultheriæ.....	℥ i	
	Liq. calcis.....	ad. ℥ vi	

M. Ft. emuls.

69

R.	Tinct. hyoscyami.....	℥ iss	The alcohol in the tincture will
	Potass. citratis.....	℥ iss	cause separation of potassium citrate
	Aquæ.....	ad. ℥ iii	solution. Use mucilage of acacia (or of
M.	Ft. sol.		tragacanth) to dissolve the citrate and
			a smooth emulsion is obtained.

70

- R. Heroin hydrochlor..... gr. i
 Ammon. carb..... 3 i
 Terpini hydratis..... gr. xlviii
 Syr. prun. virg..... 3 vi
 Aquæ chloroformi....ad. 3 viii

Triturate the terpin hydrate with the ammon. carb. to a *fine* powder, add 45 grains of powdered tragacanth and then 7 oz. of water. Triturate to a smooth mixture and add the rest of the ingredients.

71

- R. Guaiacolis..... 5 cc.
 Eucalyptolis..... 12 cc.
 Iodoformi..... 4 Gm.
 Olei olivæ.....ad. 100 cc.
 M. Ft. solut. Sig.—For hypodermic use.

Use only a neutral (or nearly so) olive oil and sterilize it by heat. Dissolve the other ingredients in it while warm, and filter if necessary.

72

- R. Sodii bromid..... 30.00 cc.
 Tr. cannabis ind..... 15.00 cc.
 Elix. aromat.....ad. 120.00 cc.
 M.

Dissolve the sodium bromide in about 50 cc. of aromatic elixir. Mix the tincture with an ounce of strained honey and add this gradually to the bromide solution with shaking. Then add enough elixir to make 120 cc.

73

- R. Sodii bromidi..... 3 iv
 Fldext. hyoscyami..... 3 ii
 Fldext. lobeliæ..... 3 ii
 Fldext. pulsatillæ..... 3 xv
 Fldext. lupulini..... 3 iv
 Aquæ destillat.....ad. 3 iv
 M.

The lupulin acts badly in such a mixture. Mix the fluidextracts, add four drachms of honey, then gradually add 1 ounce of water with vigorous shaking. Dissolve the sodium bromide in 1 oz. of water, add gradually, then add water to make 4 ounces.

74

- R. Luminal sodium..... 3 i
 Tr. cannabis indic..... 3 v
 Elix lactopeptin.....ad. 3 iv
 M. Sig.—Teaspoonful as directed.

Use 3v honey to emulsify the tincture of cannabis.

75

- R. Argyrôl..... 3 ii
 Bals. Peru..... 3 ii
 Mucil. acaciæ..... 3 i
 Olei olivæ.....ad. 3 vi
 M. Sig.—For external use.

Dissolve the argyrol and 3ss of soft soap in the mucilage, by aid of a gentle heat, gradually add about 2 1/2 ounces of olive oil with shaking, then the Peru balsam in the same way, and finally enough oil to make 6 fluidounces.

76

- R. Ol. cadini..... 3 i
 Calaminæ præp..... 3 iv
 Zinci oxidi..... 3 iii
 Aq. hamamelidis..... 3 ii
 Aquæ destillat.....ad. 3 vi
 M. Ft. lotio.

Mix the oil, calamine and zinc oxide with 30 grains of powdered tragacanth, add 3 ounces of water and make an emulsion. Then add the rest of the ingredients. Or about 30 minims of tincture of soft soap may be used.

77

- R. Calaminæ præp..... 3 i
 Zinci oxidi..... 3 ii
 Adipis lanæ..... 3 i
 Liq. calcis.....ad. 3 vi
 M.

Add about two drachms of tincture of soft soap—or one drachm of soft soap, and emulsify. The lanolin cannot absorb all of the lime water.

78

- R. Resorcinol..... gr. xx
 Zinci oxidi..... ʒ iv
 Acidi borici..... gr. xx
 Olei olivæ..... ʒ ii
 Liq. calcii hydrox..... ʒ vi

M. Sig.—For external use.

Dissolve the resorcinol in the lime water, add the olive oil and shake until well emulsified. Then sift in the zinc oxide, and finally incorporate the boric acid by triturating with a little of the mixture before mixing all.

79

- R. Olei cajuputi
 Olei cadini
 Olei terebinth.....aa ʒ ii
 Tinct. capsici
 Aq. ammoniæ.....aa ʒ iv
- M. Ft. linim.

Spirit of ammonia should be used. An emulsion is impracticable.

80

- R. Petrolati liq. pond
 Magmae magnesiae.....aa ʒ ii
- M. Ft. emuls. Sig.—One tablespoonful as needed.

81

- Liquid petrolatum..... 60 cc.
 Mucilage of agar, 2 per cent 60 cc.
- Sig.—Agar Emulsion.
 (Prof. G. A. Bergy)

Prepare the mucilage of agar by dissolving 1.2 Gm. of agar in 60 cc. of boiling water. Transfer to a mortar and allow to cool to 45° C. Warm the liquid petrolatum to 45° C. and gradually incorporate it with the mucilage, preferably using an egg beater. Continue the beating (or trituration) until the emulsion is cold.

(Makes a stiff jelly-like emulsion which will not pour.)

82

- R. Magmae magnesiae..... ʒ i
 Magmae bismuthi..... ʒ i
 Petrolati liquidi, pond..... ʒ i
- M. Ft. emuls.

Mix the magmas, and gradually add the liquid petrolatum, with vigorous shaking. (Prof. G. A. Bergy.)

Mayonnaise Dressing (Prof. G. A. Bergy)

83

- Salad oil..... 350
 Yolk of eggs..... No. 2
 Sodium chloride..... 4.0
 Powdered sugar..... 2.5
 Powdered mustard.... 1.0
 Powdered black pepper 0.5
 Powdered capsicum.... 1.0
 Powdered paprika..... 0.25
 Curry powder..... 0.25
 Mace, ground..... 0.25
 Water..... 8.0
 Vinegar..... 16.0

Mix the condiments and triturate to a very fine powder (important). Add the carefully separated yolks of two eggs, 4 cc. of water and 4 cc. of vinegar, and mix well. Then incorporate 240 cc. of the oil gradually, adding 10 cc. at a time and using an egg beater or mechanical emulsifier. Now dilute the remainder of the vinegar with the remaining 4 cc. of water, and continue the addition of oil, alternating with small portions of the vinegar mixture until all has been added. The beating should be vigorous throughout, and the finished dressing should be smooth and very thick. Vinegar, lemon juice etc. cause thinning of mayonnaise. Prof. Bergy prefers refined corn oil (Mazola) for the above, but olive or other salad oil may be used.

Ayerst Mayonnaise

Cod Liver Oil Mayonnaise

84

Egg yolks.....	No. 2
Fresh lemon juice.....	3 iii
Cod liver oil (best quality)	0 i
Sodium chloride.....	3 ss
Water.....	3 i
M. s. a.	

Beat the egg yolks and lemon juice together and gradually add the cod liver oil beating thoroughly. Dissolve the sodium chloride in the water and mix with the emulsion. Best results are obtained if the eggs and oil are chilled before mixing. (Prof. R. O. Hurst, Ont. Coll. Pharm.)

Prescriptions from State Board Examinations

FOR CRITICISM AND PRACTICE

I		2	
R.	Olei morrhuae..... 50 c.c.	R.	Chloroformi..... 4 c.c.
	Acaciae gran..... q. s.		Ol. amygdal dulc..... 6 c.c.
	Syrupi..... 10 c.c.		Syrupi tolut
	Ol gaulther..... 4 c.c.		Aqua dest. aa q. s. ad. 100 c.c.
	Aqua..... q. s. ad. 100 c.c.	M.	Ft. emulsion. (Tex.)
M.	Ft. emulsion. (Tex.)		
3		4	
R.	Olei. terebinthinae..... 3 i	R.	Oleores. aspidii..... 3 ii
	Olei limonis..... gtt. vi		Emuls. ol. ricini..... 3 ii
	Syrupi..... 3 iv		Syr. simpl..... ad. 3 iv
	Aqua cinnamomi..... ad. 3 ii	M.	Sig.—3 i q. three hours. (N. C.)
M.	Sig.—Teaspoonful every two hours. (N. C.)		
5		6	
R.	Ammoniaci..... 4.0	R.	Chloroformi..... 4.0
	Tr. opii. camph..... 8.0		Ol. amygdal exp..... 6.0
	Aqua dest..... 100.0		Tragacanthae..... 1.0
M.	Ft. emuls. Sig.—Coch. parv. hora post cibos. (N. Y.)		Aqua..... ad. 100.0
		M.	Sig.—8.0 four times a day. (Col.)
7		8	
R.	Ext. filic liq..... 3 i	R.	Ol. ricini..... 3 ii
	Pulv. tragacanth..... gr. x		Pulv. acaciae..... q. s.
	Sp. menth pip..... gtt. x		Syr. simp..... 3 ii
	Aqua..... ad. 3 iii		Aq. cinnam..... ad. 3 viii
M.	Ft. mist. Sig.—Dimid pro dosis sum. (Br. Col.)	M.	Ft. emuls. Sig.—Coch. ampl. primo mane. (Br. Col.)
9		10	
R.	Ammon. chlor..... 2.00	R.	Petrolati albi..... 5.0
	Terpini hydrat..... 3.00		Olei amygdal exp..... 25.0
	Fldext. buchu..... 4.00		Acaciae..... 5.0
	Aqua..... q. s. ad. 30.00		Tragacanthae..... 2.5
M.	Sig.—3 i three times a day. (N. Y.)		Syrupi..... 10.0
			Tinct. limons cort..... 1.5
			Aqua..... q. s. ad. 100.0
		M.	Ft. emuls. (Mass.)
11		12	
R.	Potass. chlorat..... gr. xxx	R.	Emulsionis Terebeni
	Tinct. myrrhae..... 3 iv		12 per cent..... 90.0
	Glycerini..... 3 i		How much terebene in each fluid-ounce? (Ill.)
	Aqua q. s..... 3 iii		
M.	Sig.—Use as gargle. (Tex.)		

13

- R. Emuls. chloroformi..... ̄ i
 Sig.—̄ i t. i. d. p. c. (Ill.)

15

- R. Emuls olei ricini 25 per cent ̄ iv
 Sig.—As directed. (Neb.)

17

- R. Olei ricini,
 Spir. æth. nit.,
 Tinct. opii camph.,
 Pulv. acaciæ,
 Sacchari..... āā 12.0
 Liquor calcis..... ad. 90.0
 M. Sig.—Teaspoonful three times a
 day. (N. Y.)

19

- R. Emulsio olei ricini 40 per cent ̄ iii
 Fiat. sec. art.
 M. Sig.—̄ iv pro re nata. (Ill.)

21

- R. Sodii benzoatis..... 0.8
 Camphoræ..... 0.2
 Olei ricini..... 15.0
 Elix aromat..... 8.0
 Aq. menth pip..... ad. 60.0
 M. Sig.—Cochleare parvum omni
 tertia hora.

23

- R. Ol. morrhuæ..... 50
 Pulv. acaciæ..... 13
 Syrupi..... 10
 Methylis salic..... i
 Aquæ..... ad. 100
 M. Ft. emuls. (N. C.)

14

- R. Olei terebinthinæ rect..... 15.0
 Olei amygdalæ exp..... 5.0
 Syrupi..... 25.0
 Acaciæ pulv..... 15.0
 Aquæ destillat ad..... 100.0
 M. Ft. emuls. Sig.—Cochleæ parv.
 ter in die. (Ill.)

16

- R. Olei morrhuæ..... 50.0
 Acaciæ..... q. s.
 Ol. gaulther..... 4.0
 Syrupi..... 10.0
 Aquæ ad..... 100.0
 M. Ft. emuls. (Ill.)

18

- R. Bromoformi..... 2.0
 Syrupi..... 20.0
 Aquæ foeniculi..... 40.0
 M. Ft. mist. Sig.—A teaspoonful
 three times a day. (Col.)

20

- R. Terebeni..... 4.0
 Extracti hyoscyam..... 0.5
 Pulv. acaciæ..... q. s.
 Syrupi tolu..... 45.0
 Aq. menth pip..... ad. 120.0
 M. s. a. Sig.—Cochleare parvum
 omni tertia vel quarta hora. (N. Y.)

22

- R. Potass acet..... ̄ vi
 Ol. santali..... ̄ iv
 Syr. acaciæ..... ad. ̄ iv
 M. (N. C.)

24

- R. Olei terebinth rect..... 9.0
 Olei amygdal. exp..... 3.0
 Acaciæ..... q. s.
 Syrupi..... 15.0
 Aquæ dest..... ad. 60.0
 M. Ft. emuls. Sig.—Cap coch. parv.
 q. q. ter vel quart. hora. (Col.)

CHAPTER VII

CONFECTIONS, ELECTUARIES, JELLIES

Confection (Lat. *Confectio-onis*), a paste or mass composed of medicinal agents with saccharine and flavoring matter, intended to be eaten, or dissolved in the mouth. Small lumps, of a size approximating some familiar object, are directed to be taken at a time. They are dispensed in jars, wide-mouthed bottles or impervious boxes.

Conserves (Lat. *Conserva-æ*), a confection containing only *fresh* (undried) medicinal agents. These must con-

tain enough saccharine matter to act as a preservative.

Electuary (Lat. *Electuarium-ii*), a confection containing *dried* medicinal agents.

Jelly (Lat. *Gelatinum-i*), a glutinous translucent substance, intermediate between a liquid and a solid, intended (*a*) either to be swallowed from a spoon or (*b*) for external application. The latter are often opaque. (See under plasmas.)

CONFECTIONS.—This term now includes both the true conserves and the electuaries, the latter terms being used rarely.

These preparations are less frequently demanded than formerly, having been displaced by lozenges. A class of preparations called “pastes” were also in use, which differed from the confections in containing gum, and in being of a firmer consistence, more like the pastilles or tabellæ of the present.

Jujube paste was made by dissolving 3 ounces of acacia in 4 fluid-ounces of water, adding 3 1/2 fluidounces of syrup, evaporating to a very thick consistence and adding toward the last 1 fluidounce of orange flower water. The warm mass was then run into shallow pans to cool and stiffen, medicinal agents, flavoring, coloring, etc., being added while still fluid. This is cut into sheets or squares and forms the so-called “jujubes” of pharmacy.

They are still somewhat in demand in France.

The true confections are made by beating the moist drug (fresh rose-petals, etc.) with sugar until a smooth mixture is obtained, a little excipient being added at the last if needed.

Electuaries offer no difficulties in preparation. The dry powders are mixed in the usual manner by trituration or sifting, then the excipient is worked in so as to form a mass.

Honey or syrups are the most common excipients. For laxative electuaries the pulp of prunes, tamarinds, figs, currants, etc., are agreeable massing agents, and aid, to some extent, in the action of the electuary.

These are prepared by steaming the fruits until they are well softened, then rubbing through a sieve to remove the skins and seeds. Currant and prune pulps are particularly agreeable as excipients.

Jellies for internal use are confined almost entirely to the administration of fixed oils, wherein they have the advantage of diminishing the adhesion of these to the mouth, and thereby lessening their taste and nauseating qualities.

Castor oil or cod-liver oil may be administered in this way. The following formula for the preparation of these is taken from Parrish's Pharmacy.

Take of the fixed oil.....	1	ounce.
Honey and syrup, each.....	1/2	fluidounce.
Powdered gum arabic.....	2	drachms.
Russian isinglass.....	40	grains.
Aromatic water (bitter almond, orange flower, cinnamon, etc.)....	6	fluidrachms.

Dissolve the isinglass by aid of heat in one-half ounce of the water, triturate the other ingredients into a homogeneous mixture with the remaining portion of the water in a warm mortar, then form an emulsion by adding the solution of isinglass, stir as it cools, and set aside to gelatinize.

Isinglass is the best base for oils, while gelatin, Irish moss, starch, salep, and tragacanth, are used for aqueous and alcoholic bodies, or for insoluble powders.¹

In order to obtain perfectly clear and transparent jellies filtration is usually necessary, and gelatin or Irish moss must be used. The other agents give opaque jellies, and do not admit of filtration.

When sugar is added, as is usually the case, it may serve as a vehicle for diffusing insoluble bodies, or such as are incompatible with aqueous fluids, as volatile oils, tinctures, etc.

When flavored with fruit juices less gelatin is needed, as the pectin in the juice gelatinizes when boiled. The "Art of Dispensing" directs these to be made by combining the juice with half its weight of sugar, boiling, skimming and straining.

To 100 parts of the hot juice are now added 2 parts of gelatin, and, after dissolving the latter, the jelly forms on cooling.

CONFECTIONS, JELLIES, ETC.

I

- R. Rose in fine powder..... 80 Gm.
 Sugar, in fine powder... 640 Gm.
 Clarified honey..... 120 Gm.
 Stronger rose water.... 160 cc.
 M. Sig.—Confection of rose.
- "Rub the rose with the stronger rose water, previously heated to 65° C. (149° F.), then gradually add the sugar and honey, and beat the whole together until a uniform mass results."
 Make one-twentieth the quantity.

2

- R. Olei morrhue..... ʒ v
 Ichthyocollæ..... ʒ ij
 Sacchari..... ʒ iss
 Olei amygdalæ amaræ..... m. iv
 Olei pimentæ..... m. iv
 Olei cinnamomi..... m. ij
 Aquæ..... ʒ iv
 M. Sig.—"Cod-liver Oil Jelly."
- Place the oil, isinglass and water in a capsule, heat upon a water-bath until the isinglass melts, then add the sugar, previously triturated with the essential oils, remove from the heat and stir as it thickens. When cold a firm jelly results.

3

- Confectio opii (U. S. P. 1860).
 R. Opium..... ʒ ivss
 Aromatic powder..... ʒ vj
 Clarified honey..... ʒ xiv
 M.

¹ For proportions needed to jellyfy see pages 265 and 307.

4

- R. Senna, in fine powder... 100 Gm.
 Cassia fistula, bruised... 160 Gm.
 Tamarind..... 100 Gm.
 Prune, sliced..... 70 Gm.
 Fig, bruised..... 120 Gm.
 Sugar in fine powder... 555 Gm.
 Oil of coriander..... 5 Gm.
 Water, a sufficient quantity to make..... 1000 Gm.
- M. Sig.—Confection of senna.

Digest the cassia fistula, tamarind, prune and fig in a close vessel with 500 cc. of water for three hours. Rub the pulpy mass, first through a coarse sieve, and then through a muslin cloth. Mix the residue with 150 cc. of water, digest the mixture for a short time, treat it as before, and add the strained product to the pulpy mass first obtained. Then, by means of a water-bath dissolve the sugar in the pulpy liquid, and evaporate the whole, in a tared vessel, until it weighs 895 Gm. Lastly, add the senna and the oil of coriander, and incorporate them thoroughly with the other ingredients while they are yet warm."

Make one-twentieth the quantity.

5

Conserva Amygdalarum. (Conserve of Almond.)

- Sweet almond..... 30 Gm.
 Powdered acacia..... 5 Gm.
 Powdered sugar..... 15 Gm.

Blanch the almond, and incorporate thoroughly with the other ingredients.

(This is a convenient mixture for the quick preparation of emulsion of almond, which may be made by triturating the above with enough water to make 500 cc. It keeps fairly well in closely stoppered bottles, and may be made almost permanent if the almonds are dried at a low heat, after blanching and bruising them.)

6

- R. Iodoformi..... gr. iij
 Ætheris..... ʒ j
 Carbon ligni..... ʒ i
 Glycerini..... ad. ʒ iss
- Ma. Ft. elect.
 Sig.—For Diarrhœa.

Dissolve the iodoform in the ether and mix with the powdered charcoal. Allow ether to evaporate and then make into a paste with glycerin.

7

- R. Potassii chloratis..... ʒ iv
 Ext. glycyrrhizæ pulv..... ʒ iv
 Pulveris cubebæ..... ʒ ij
 Olei gaultheriæ..... gtt v
 Confect. rosæ..... ʒ j
 Glycerini..... q. s.
- M. Ft. electuarium. Sig.—Take a piece about the size of a pea.

8

- R. Sulphuris..... ℥ ij
 Potassii bitartratis..... ʒ j
 Sacchari..... ʒ j
 Syrupi fuscii..... q. s.
- M. Fiat electuarium.
 Sig.—"Sulphur and Cream of Tartar."

9

- R. Tinct. ferri chlorid..... ʒ ij
 Mucilaginis acaciæ,
 Syrupi..... aa ʒ vij
 Tinct. vanillæ..... ℥ xv
- M. Sig.—"Iron Jelly."

Mix the mucilage, syrup and vanilla and add the tincture of iron. If the mucilage is fresh, the mixture sets into a ruby-red, transparent jelly, but an old mucilage requires a larger proportion of mucilage. This jelly is liquefied by acids.

10

R.	Olei ricini.....	90	Dissolve the sodium hydroxide in the
	Acid stearici.....	4.2	alcohol and add the stearic acid and
	Sodii hydroxidi.....	0.6	castor oil. Heat until combined and
	Saccharini.....	0.1	add the other ingredients.
	Olei menthæ pip.....	0.2	
	Alcoholis.....	5.0	
M.	Sig.—“Castor oil jelly.”		

11

Castor Oil Caramels

	Castor oil.....	12 oz.	Dissolve the sugar in the water and
	Glucose.....	16 oz.	add the glucose, chocolate, and magne-
	Confectioner's sugar....	23 oz.	sium carbonate. Heat to boiling and
	Oil of wintergreen.....	30 min.	add the castor oil. Stir well and boil
	Carbonate of magnesia..	240 gr.	down to caramel consistency, then add
	Chocolate.....	2 oz.	the flavor and make 96 caramels.
	Water.....	26 oz.	

12

R.	Thymolis.....	0.25	Soften the gelatin by soaking in the
	Eucalyptolis.....	0.50	water, then add the glycerin and heat
	Methylis salicylatis.....	0.50	until the gelatin is dissolved. Add the
	Olei menthæ viridis.....	0.50	carmine solution, cool to about 50° C.,
	Chloroform.....	0.50	then add the mixed aromatics, mix
	Liq. carmini.....	0.02	thoroughly and pour into a frame made
	Gelatini.....	15.00	by placing brass candy-bars on a glass
	Glycerini.....	37.50	plate so as to form a rectangular enclo-
	Aquæ.....	37.50	sure 3 X 6 inches. When cold, cut
M.	Ft. pastil No. xxviii		
	Sig.—Aromatic pastilles (Bergy.)		
			by $\frac{3}{4}$ in.

CHAPTER VIII

PILLS

The word "pill" comes from the Latin *Pilum*—a ball, and the diminutive *Pilula*, a little ball, is the term used in prescription-writing to denote a pill or pills. A pill may be defined as a mass of medicinal matter, round or ovoid in form, intended for internal administration. A pill should weigh, exclusive of coating, from one to five grains, none being less than one grain unless specially ordered.

A Bolus Lat., *Globulum*, is a large pill, commonly more than five grains. When very large they are preferably made oval-form. They are more generally prescribed in veterinary practice, and should always be just firm enough to keep their shape without being hard.

Dragees are sugar-coated boli.

Granules Lat., *Granula*, are sugar pellets impregnated with medicinal matter which is applied in liquid form and absorbed by the pellets; these are afterward dried. They are restricted mostly to homœopathic practice, and are sometimes called pellets.

Parvules Lat., *Parvulae*, are very small sugar-coated pills, usually containing powerful remedies in small doses, and colored red or pink to

distinguish them from granules.

Compressed pills are more properly tablets, and will be treated under that head.

Aggregation pills are made by the gradual accumulation of medicinal ingredients upon a prepared nucleus. They are treated under the head of sugar-coating.

Concentric pills consist of successive layers of medicinal matter, each of which has a different medicinal action from the others, and is separated by a coating of sugar, tolu, etc. They are intended for combinations of drugs, one of which is best absorbed in the stomach and another in the intestines, the latter forming the inner ring or nucleus, and being coated with tolu, salol or colloidion, while the outer dissolves in the stomach. They have been also proposed for administering bodies which unite if mixed, as the ingredients of Blaud's pills, the two being separated by a coating of suitable material. They are very troublesome to make and are seldom demanded.

Enteric pills Lat., *Pilulae tunicatae*, are pills coated with a substance that will not dissolve in the stomach, but dissolves in the intestines.

The importance of pill-making in pharmacy is suggested by the popular phrase often used to designate a pharmacist—"a pill-maker."

Not only is the making of pills important, but the knowledge and skill which the pharmacist exhibits in making various pills may commonly be taken as a criterion of his knowledge and skill in general pharmacy.

The operator who treats all pill-masses alike, uses the same excipient and methods in each case, shows a woeful lack of knowledge or of judgment, and usually of both. The science of pill-making involves a knowledge of chemistry, materia medica, and pharmaceutical physics, and cannot be thoroughly learned without this knowledge. Skill in manipulation is also necessary, and can only be acquired by practice coupled with judgment.

Study and practice then are the only avenues by which the pharmacist can hope to become master of the art of pill-making.

The object of prescribing medicines in pill-form is two-fold; to cover the taste of disagreeable remedies, and, in some cases, to give them in a concentrated form.

Any medicine which may properly be administered in solid form, and the dose of which is not too bulky, may be prescribed in the form of pills. Many drugs are too bulky to administer in this way, and some, such as the salts of bismuth, cerium, etc., do not have as good a therapeutic action if taken in this form. A few salts, as the bromides of potassium, sodium, etc., have an irritant action, and should always be administered in solution.

Many salts are so easily dissolved as to present special obstacles to the forming of good pills, and many liquids are prescribed in pill-form which render the problem more complex. It is in the ingenuity and judgment displayed in the handling of such special cases, and in the combinations of difficulties that the skill of the operator is best shown.

Special precautions are sometimes to be observed in weighing and mixing the ingredients of pills. Solid extracts should be weighed upon a piece of paper upon which a little lycopodium has been sprinkled and the whole counterpoised. This prevents sticking of the extract to the

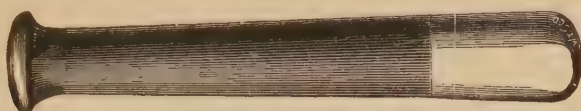


FIG. 9.—Pill pestle.

paper and avoids loss. If the extract be hard or tenacious, unless dry enough to be powdered, it should be softened by trituration with a little water or diluted alcohol (strong alcohol is in most cases not so good for this purpose), taking care to add only enough to make a thick liquid with the extract. This will now be in a condition to mix readily with powders or other extracts. Potent remedies, the alkaloids, active principles, etc., are first mixed with other powders, or if mixed with extracts they may first be dissolved in a few drops of the liquid used to soften the extract to insure complete admixture. Resinous extracts are softened by triturating in a warm mortar or working on a warm plate, which should not be hot.

The ingredients of the pills having been thoroughly mixed, they are next to be formed into a stiff paste or dough for shaping into pills. This is called a *pill-mass*.

The body added to form the mass is called the *excipient*.

A good pill mass is *plastic, adhesive*, but not sticky, and *not easily changed* under ordinary conditions, except by drying.

When well made it is easily moulded and does not adhere to the hands or utensils.

When formed into pills, these should dissolve or crumble when placed in warm water for a few minutes.

The choice of a mortar is important in making a pill-mass. A wedgewood mortar with a broad base, and a small pestle having an extra long and stout handle, should be chosen.

Triturating the mass will be found much less easy and effective than kneading it. By holding the pestle so that the end of the handle rests upon the fleshy portion of the hand near the wrist, the mass can be easily and rapidly worked and nearly the entire weight of the operator imposed upon it without fatigue. The heat generated in working is often an important factor in forming the mass. The warmth of the hands is often well taken advantage of also, by kneading in the hands.

Some operators prefer to use a glass or porcelain slab and a broad and stiff spatula or putty-knife in forming the mass. This has the advantage of forcing more material under the action of the knife at



FIG. 10. — Pill spatula.

one time, and more rapid work may be done upon particular masses, but it has many disadvantages, being restricted in range and more laborious.

An iron plate or griddle well smoothed and polished is a good adjuvant to the pill utensils, being easily and quickly warmed, and serving an excellent use, when warm, in working resinous or tenacious masses.

The mass should be worked very thoroughly and a free use made of the spatula to keep the mixture under the pestle. The sides of the mortar and pestle should be scraped frequently while the mass is being formed. A stiff spatula is better here than a limber one. The stubs of broken spatulas, the broken and ragged edges being ground off and rounded, are especially useful in pill-making.

The mass being formed, we have next to **divide and shape it into pills**.

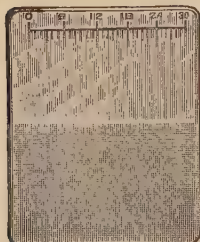


FIG. 11. — Pill tile.

It is first taken from the mortar or tile as completely as possible and worked in the hands into a short cylinder, then by means of a broad spatula or wooden roller it is rolled on the tile or pill machine until its length corresponds to the number of divisions upon the tile or machine representing the number of pills we wish to make.

Care must be taken here to keep the "pipe," as it is called, of uniform diameter throughout, and the ends must be squared up frequently by pressing them up with the spatula. This is a very important part of the operation.

The pipe is then placed upon the divisions and cut into sections.

If cut upon a tile, care must be taken to hold the spatula at right angles to the pipe, and to cut all evenly or there will be a difference in the sizes of the pills. The sections of pipe are then rounded roughly in the fingers and finished by rolling under the finisher. In absence of a pill-finisher a large specie cork may be used, or the clean cover of an ointment box, the sides of the cover having been cut down so as not to touch the tile when resting upon the pills.

A duplex finisher is to be preferred to a single finisher, as being better adapted to pills of different sizes.

When rounding the pills in the fingers, they should be pressed, not folded into shape, to avoid showing a crease in the pills. Such creases are difficult to eradicate.

If the pills show a tendency to crumble or show folds when finishing, a smooth surface may be obtained by placing a single drop of water, syrup or diluted alcohol upon a warm tile, and rolling the pills in this under the finisher.

A small, thin, iron plate is very convenient for this purpose, since it can be more easily and quickly warmed than glass or porcelain.

CONSPERGENT OR DUSTING POWDERS

These are used to prevent the mass from sticking to the machine or to prevent the pills from adhering to each other in the box.

They should be used sparingly in all cases, and particularly when the pills are to be coated.

Many masses can be made into pills without the use of a dusting powder, but most masses require a little.

Lycopodium is most frequently used.

The spores of lycopodium have on the surfaces microscopic ridges or hair projections which cause the spores to cohere in a manner similar to burdock burrs, and form a chain-like coating around the pill if it be too moist. Thus a little lycopodium will accomplish as much as a considerable quantity of another absorbent powder and the excess can readily be poured off.

Powdered licorice root is often used. This is a good absorbent and has the advantage of a pleasant taste. The peeled or Russian powdered licorice should be selected for this purpose, being brighter in color and more palatable.

For white pills a white dusting powder is to be preferred. Powdered starch answers well for this purpose. Powdered orris root may also be used, or talcum.

For pills containing odorous ingredients, such as valerianate of zinc, creosote, etc., or such as are particularly nauseous, an aromatic dusting powder is often agreeable. Orris root or cinnamon, or a mixture of these is a pleasant addition to the pill-box. Avoid the use of aromatic powders which contain a large proportion of natural oil, such as cardamom, fennel, nutmeg, etc. These are apt to become sticky.

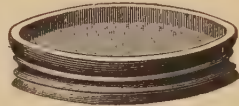


FIG. 12.—Pill finisher.

EXCIPIENTS

The choosing of an excipient is a matter of considerable importance. It is this which determines whether the pills shall be too large or as small as possible, soluble, or so slowly disintegrated as to be of little value, permanent or easily changed by action of the air. It is here that the operator's knowledge of chemistry, materia medica, and physics becomes of practical use.

The excipient should be harmless in its action upon the system, and should not be incompatible with any of the ingredients of the pill. It should have a preservative power upon the mass.

The best excipient is that which most quickly and easily makes a good mass and a small pill which is easily disintegrated.

In many cases a combination of excipients is best in order to obtain small pills, one to dissolve the substance and reduce the bulk, the other to impart adhesiveness and plasticity to the mass. This point is often overlooked in the quest for a "universal excipient," which can never be found. Many of these so-called universal excipients will make a plastic mass for a large variety of pills, but they add materially to the size of the pills instead of decreasing them, as can often be done.

Excipients may be divided into three classes, liquid, dry and adhesive excipients.

LIQUID EXCIPIENTS form the most important class and are most frequently used.

They are used for all bodies which are soluble to some extent in the ordinary solvents, including vegetable powders and their extracts, soluble salts, etc. Some of these are soluble in water, and some only in alcohol or oils, etc., and the choice of excipient is controlled by these considerations.

The excipient should have some solvent power upon the solid which is formed into a mass. Thus, we cannot form camphor into pills by use of water because the water has not the solvent power to soften and render adhesive the camphor, but if we use a little castor oil the camphor is partially dissolved, the remainder rendered soft and plastic and the mass can be rolled into pills.

On the other hand, not all good solvents make good excipients. Alcohol and ether are good solvents for camphor, but very poor excipients for it, because they are too volatile, and the solutions are limpid and possess no adhesive properties. A solvent excipient should either be somewhat viscid and sticky of itself, or it should make a solution by action upon the pill-ingredients which will possess enough of these properties to bind the remaining solids in a plastic mass.

Excipients should be added cautiously and well worked in, or the mass may suddenly become too soft. When first added the mass may appear quite dry and crumbling, after a moment's trituration, but on continued kneading the solvent power of the excipient becomes manifest, more liquid is formed than was added in the first place, owing to the fact that a portion of the solid has entered into solution, and a good mass may be formed without further addition of excipient.

It is generally a saving of time and labor, and oftentimes a better mass is secured, by adding all of the required excipient at once, but this plan calls for considerable experience and judgment. The novice who attempts it is almost sure of getting in too much and spoiling his work. Practice will enable one to judge quite closely, particularly in the use of excipients to which one is accustomed. The excipient is best dropped upon the blade of a spatula and transferred to the end of the pestle (not the side), from whence it can most easily be distributed through the mass.

A free use of a spatula should be made in keeping the ingredients in the bottom of the mortar and in removing what has caked upon the end of the pestle. The spatula which is used for this purpose should not be dipped into the excipient jar, or this will become contaminated.

The most important of the liquid excipients are glucose, honey, syrup, water, tinctures, alcohol, glycerin, oils, soap and water, treacle and soft extracts.

Glucose, honey, syrup and water are adapted for those bodies soluble in water and for many vegetable powders. Sometimes water is used first to partially dissolve and reduce the bulk, then glucose to make the mass.

Glucose or honey is better than syrup, being more viscid and adhesive.

Glucose usually contains a quantity of dextrin, formed during the process of manufacture, which adds to its value as an excipient. It has been improperly called "Syrup of Dextrin."

The commercial glucose is very thick and for most masses is best diluted, when it adds less to the bulk of the pill. A mixture of about four parts of glucose and one part of syrup keeps well and is sufficiently limpid for most purposes.

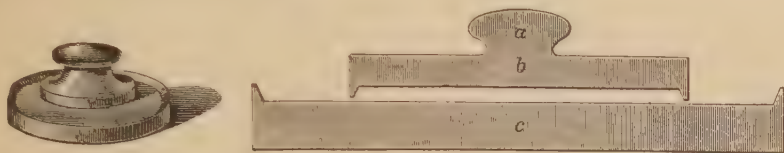


FIG. 13.—Pill finisher.

Honey contains a little wax and gummy matter which makes it more adhesive. It will not make a white pill, however, and possesses no advantage over glucose, except in consistency.

Water is little used alone as an excipient, but is valuable as an aid, as when soap is used, or in some cases with glucose, to obtain a smaller pill than could be made with glucose only.

Alcohol and alcoholic tinctures are best used with resinous bodies.

When resins of jalap, podophyllum, etc., are prescribed in pills, the respective tinctures of those drugs may be used as an excipient. They possess the advantage over alcohol alone of being more sticky and making a more adhesive mass. Tinctures of powerful drugs, as cannabis indica, nux vomica, etc., should not be used, since even the small amounts needed will add materially to the medicinal activity of the pill.

Alcohol and tinctures, however, are not in special favor as excipients, because they make a tough mass which crumbles unless worked up quickly, and the pills are apt to become very hard. These qualities may be partially obviated by use of a little glycerin with the alcohol.

Soap is better to use with resinous bodies, although it makes a larger pill. It increases the solubility of the pill and keeps the mass soft.

The water must be added cautiously to these masses, since a very small excess will make the pills so soft that they cannot be handled. The greatest objection to soap is its incompatibility with metallic salts, and with acids.

Glycerin, by reason of its wide solvent power, is much used as an excipient.

Owing to its hygroscopic nature it is little used alone, but is much used in combination with gums or starch.

It prevents the pills from becoming too hard or insoluble, but should not be used when pills are to be gelatin coated.

A good excipient, which serves for quite a wide range of masses, may be made by sifting into glycerin 4 per cent of powdered tragacanth, and allowing to stand twenty-four hours.

This resembles the official mucilage of tragacanth, which is especially valuable as an excipient for salts and insoluble bodies.

Treacle or molasses may be substituted for honey as an excipient, but is not as good and is seldom used.

Sometimes the **tonic extracts** are prescribed as excipients, particularly extract of malt, extract of dandelion and extract of gentian.

These make good masses with many bodies, and are often intended for a therapeutical adjuvant to the pill. They materially increase the

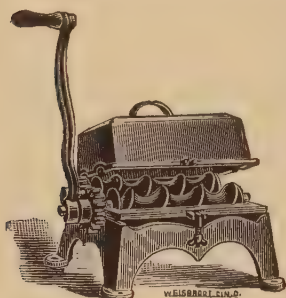


FIG. 14.—Hand-massing machine.

size of the pill, and are seldom chosen for excipients when not prescribed by the physician. They are liable to be slightly acid because most vegetable extracts are naturally acid, and may become more so from oxidation of the sugars or albuminous matter, first to alcohol, then to acetic acid. When this has occurred they are unfit for use as excipients for pills containing carbonates, bicarbonates or any body upon which the acid can act.

A strong alcohol is much less liable to oxidize to acid than a weak one, hence this trouble is seldom met with in extracts containing more than 20 per cent of alcohol.

ADHESIVE EXCIPIENTS are required for such bodies as are insoluble in the ordinary solvents and are held in shape solely by the tenacity of the excipient. Such are the salts of bismuth, arsenous acid, reduced iron, mercury, etc.

These present few difficulties, the choice depending mainly upon the relative sizes of the pills obtained. In many cases an excipient which will increase the size of the pills is desirable. It is seldom that a pill is desired smaller than a one-half grain quinine pill, and this may be taken as a standard of size for potent remedies or heavy bodies which require to be built up.

Mucilage of tragacanth is the chief excipient of this class.

Tragacanth responds quickly to the action of water and swells enormously, which causes the pills to disintegrate. The mucilage is a thick mass, well adapted to massing dense bodies, and contains enough glycerin to prevent the mass from becoming hard.

Mucilage of acacia, on the contrary, is a liquid which makes a much smaller pill, but the pills will grow so hard in a short time that they are almost insoluble. Acacia dissolves very slowly, and hence pills containing it are less quickly disintegrated, even when glycerin is present. On the whole, the use of acacia or mucilage of acacia as an excipient is not to be recommended.

Mucilage of tragacanth or other gums should not be used too freely, because if too much is added, the mass becomes elastic, rubber-like, and the pills cannot be rounded.

Confection of rose is a favorite excipient with many. This owes its adhesive powers to the sugar and honey which it contains, and possesses no advantage over these. The presence of the rose is objectionable in some cases because of its astringency, or because of possible reactions with the tannic acid which it contains. It should not be used with pills which are laxative in their action, or with those containing iron salts.

Powdered extract of licorice, with glucose, evaporated honey, or other liquid excipient, is often used.

Resin ointment, petrolatum or Canada balsam, are sometimes used as excipients where aqueous or alcoholic excipients are to be avoided.

These are little used, being confined chiefly to pills of nitrate of silver, permanganate of potassium, or very deliquescent salts.

Most of the so-called "**universal excipients**," formulas for which are published frequently, belong properly to the adhesive class.

The following are examples of these:

Starch, 10 Gm.; Glycerin, 90 Gm. Rub together in a mortar, then heat to 290° F. until the starch granules are dissolved.

Tragacanth, 4 Gm.; Glycerin, 96 Gm. Triturate together, and allow to stand twenty-four hours. (Wiegand.)

Glucose, 120 Gm.; Glycerin, 30 Gm.; Powdered Acacia, 6 Gm.; Benzoic Acid, 0.065 Gm.; mix. (Remington.)

DRY OR ABSORBENT EXCIPIENTS.—These are used to stiffen liquid or soft bodies so that they may be formed into a mass.

They are often **the most difficult excipients to select**, especially where comparatively large quantities of liquid are prescribed in pill form. Oftentimes both an absorptive powder, and a liquid excipient must be used in order to obtain a plastic mass and the pills which result are thus enlarged.

Where the liquid can be evaporated this may suffice, but many liquids do not admit of this, and it is often difficult to find a body which will combine with these to make a good pill-mass without forming too large a pill.

Magnesia has the property of absorbing large quantities of some liquids and making a gelatinous mass, and is often used in pills containing large quantities of liquid.

The light magnesia should be used for this purpose—not the heavy. If the light magnesia be mixed with fifteen times its weight of water, and allowed to stand half an hour, it sets to form a jelly which cannot be poured from the vessel. When mixed with some balsams, oleo-resins, or volatile oils, it unites with the acids of those bodies to form salts, and usually a small proportion of magnesia is sufficient to make a plastic mass. It acts best when a little water is present with the oil or balsam.

The copaiba mass of the National Formulary is made in this way—allowing the mass to stand until it has stiffened before rolling into pills. This is done in order to give time for completion of the reaction.

A serious objection to the use of magnesia lies in the fact that if too much be used the mass forms a very hard cement-like body, which

is insoluble, and in order to avoid this considerable time is required for the mass to stiffen. When the exact amount of magnesia required is known, the reaction may be hastened by slightly warming, taking care to avoid loss of volatile constituents by too high or too long-continued heating.

Were it not for this tendency in magnesia to form medicinal pebbles instead of pills, when used in excess, it would be a valuable material at the pill counter, but considered in this light it should be used very cautiously, if at all.

Not more than one part of magnesia to ten of liquid should be used in any case.

Soap has a considerable absorptive power for oils and certain chemicals. Animal soap, commonly called **curd soap**, is much better for this than vegetable or castile soap, being harder and more tenacious. Oftentimes a good mass may be made with this without the use of water, either by massing or digesting. A good creosote pill may be made by digesting equal parts of creosote and curd soap (or a larger proportion of castile soap) in a stoppered wide-mouth bottle until they combine, then allowing the mass to cool before rolling. This method was recommended by Mr. Martindale, of London. Soap is also useful as an addition to vegetable powders for massing oils, etc.

Crumb of Bread (*Mica Panis*) is an excellent absorbent for oils, and has for many years been recommended for use as an excipient.

It serves fairly well for pills, but is seldom at hand in a fresh condition in the pharmacies, and does not possess sufficient advantages over other excipients to be sought avidously. It does not make a very adhesive mass and has mostly passed into disuse.

It is best used when one day old.

Flour, either wheat or rye flour, makes a good substitute for crumb of bread when used in connection with aqueous fluids. The gluten makes plastic dough, the absorbent powers of which are interestingly shown at the Waltham watch factory, where dough is used to remove the excess of oil from the minute-screws by which the watch-works are held together, a little trick which, though simple, has been the means of saving many thousands of dollars to the company. It removes the excess of oil thoroughly, yet leaves them lubricated and in a condition to resist rust. Flour may often be substituted for starch as an excipient, with advantage.

Powdered Licorice Root is one of the best inert drying powders, and is largely used. The greatest objection to it is that too much may be required, so that the pills are unduly large. With small amounts of liquids it may be used in nearly all cases.

Powdered Extract of Licorice is particularly useful in connection with powdered licorice root.

The commercial article contains a large quantity of starchy and other insoluble material (commonly 35 to 40 per cent) which is absorptive, and a better mass may be secured than when the powdered root is used alone.

Ordinarily about half as much of the powdered extract is used as of the root.

Tragacanth has a strong affinity for aqueous liquids, but is not of so much value with oils or balsams unless a little water be added also.

Tragacanth consists of a small proportion of a soluble gum, and large proportion of Bassorin, a peculiar gummy body which swells enormously in water, but does not dissolve. It is this body which gives to tragacanth its sponge-like property, but it responds only to aqueous solvents.

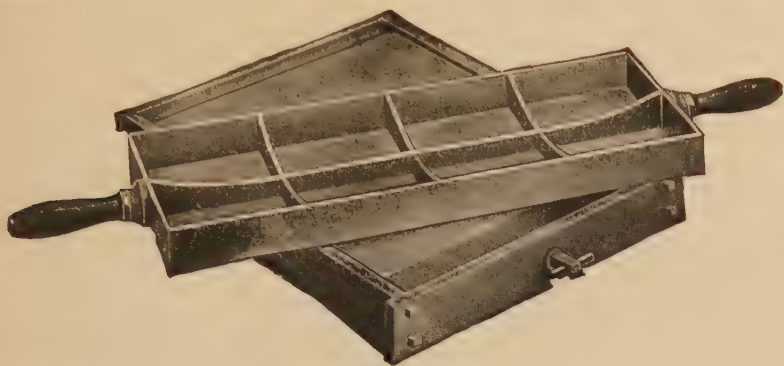


FIG. 15.—Piping machine.

Acacia is sometimes substituted for tragacanth in order to bind a mass together, but is more objectionable, unless mixed with glycerin to prevent the pills from becoming insoluble.

Powdered Althea is an excellent form of gummy excipient to use. This consists chiefly of gum and starch, and does not harden as acacia or tragacanth alone does.

It is much used in some sections.

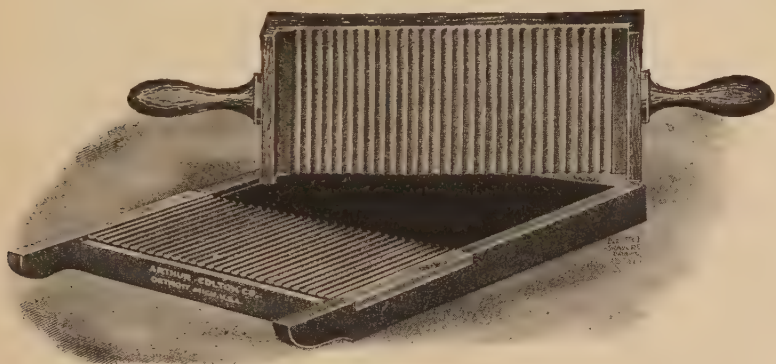


FIG. 16.—Pill machine.

Precipitated Phosphate of Calcium is the best of the inorganic powders, except magnesia. Its usefulness in this respect is limited, and it is employed rather as a diluent.

It is almost insoluble in neutral liquids, and has little or no medicinal action when taken into the system in the solid form.

Manna is seldom used. It is used as a protective, owing to its saccharine character. It may be used advantageously with salts containing water of crystallization which have a tendency to liquefy when triturated, or in those in which water is set free by chemical reaction, as in the Blaud's pills, etc.

Manna not only takes up the water, but protects the salt, and makes a fairly good mass.

Cacao Butter may be used for pills containing much oil or soft resin. The oil is usually added to the melted butter, stirred in thoroughly, and the mixture chilled until it stiffens.

The quantity of oil which can thus be incorporated is limited only by the consistence of the mass so obtained. Pills made of cacao butter cannot be handled much, and should be kept in a cool place.

Wax will absorb much more oil, and the pills made from it are more permanent.

The yellow wax is better to use, since the white contains small quantities of foreign fats which are liable to become rancid, and it has a greater tendency to crumble.

Objections are made to wax that even when mixed with a considerable proportion of oil, the fusing-point of the mixture is above the heat of the body, and the mass is insoluble in the stomach, consequently the pill will pass through the system without disintegrating.

It is claimed, however, that if the wax be first mixed with starch this will not occur, and a mixture is recommended as a stock-excipient of equal parts of wax and starch, or flour. In making it the wax should first be obtained in thin shavings, dried for a few days in a warm place, then triturated lightly with the starch or flour in a cold mortar. It is important that the mortar be well chilled, and kept so by being placed in a basin of ice water.

Creosote, phenol, volatile oils, balsams, oleo-resins, etc., can now be incorporated with this base and rolled into pills.

This mixture of powdered wax and starch is rather difficult to make, and the same result may be obtained by melting the wax, then adding half its weight in flour or licorice root, and *half* the balsam or oil, then when nearly cold incorporating the remainder of the balsam (or oil). Balsams and liquid oleo-resins usually require about one-third their weight of wax (together with the flour or licorice root), and oils, and other similar bodies require one-half to two-thirds their weight in wax in order to form a good mass. Much depends upon the consistency of the oil or balsam, in determining the proportions to be used.

CLASSIFICATION OF PILLS

The following classification of pills according to their ingredients is a modification of that made some years ago by Mr. Joseph Ince, Lecturer on Pharmacy at the School of Pharmacy of the Pharmaceutical Society of Great Britain.

The classification is made for the purpose of discussing special difficulties and the best excipients for each class, but it should be borne in mind that the excipients mentioned are but for that class only, and that combinations of ingredients from the different classes call for the exercise of judgment in order to select the best for the combination at hand.

CLASS I.—POWDERED DRUGS AND VEGETABLE EXTRACTS

These offer very few difficulties, and with most of them any of the liquid excipients will make a good mass, since most vegetable powders are adhesive when wet. If the drug is of resinous or oily nature, soap or an alcoholic tincture of the drug, or glycerin, is to be preferred. In all cases it should be remembered that powdered drugs *absorb moisture slowly*, and time is required to obtain a satisfactory mass.



FIG. 17.—Pill mass rolls.

The mass may be made quite soft at first, and will stiffen as the pills are being rolled. If the mass be too hard the pills are liable to crumble and require remassing.

The same applies to extracts, but in a less degree. Since extracts are required to be of a "pilular consistence" they are sometimes ready to be rolled immediately, but more often they are either too hard, and require to be softened with alcohol or water, or are too soft and may be evaporated on a hot plate, or stiffened by incorporating powdered licorice, etc.

Sometimes a little gum becomes necessary, when althea or tragacanth are to be preferred.

Aqueous extracts are sometimes found in a condition of partial fermentation, acetic acid and carbonic acid gas being slowly formed. Such require to be evaporated on a hot tile, before being incorporated into pills, lest the pills afterward fall apart from pressure of the gas or reaction of acid with other ingredients. The heat stops the fermentation and drives out all of the gas. These extracts (and several of the official solid extracts are aqueous) should never be used in pills containing carbonates, unless first tested and proved to be free from acid. The acetic extracts should also be avoided in such pills.

CLASS II.—ALOE, RESINS, AND GUM-RESINS

This class would include all inspissated juices, as opium, etc., and non-oleaginous exudations. They are all solid but non-fibrous bodies, largely soluble in mixtures of alcohol and water, and make small, easily soluble pills.

Soap and water head the list of excipients for these, about one part of soap to six to twelve parts of drug being required according to its character. Soap increases the solubility of resinous bodies and the mass remains soft. Solution of potassa was formerly used to a considerable extent with these, forming a soap with the resin, but the medicinal properties are somewhat altered by such treatment, and its use is now universally condemned.

Compound decoction of aloe, with or without soap, is a favorite excipient in England for this class, and makes an excellent mass. Liniment of soap or of soft soap might serve in that capacity when the odors of rosemary or lavender are not objectionable.

When soap is incompatible with other ingredients, glycerin, mucilage of tragacanth, oil, or glucose, may form a good mass.

Alcohol makes a tough mass which hardens rapidly.

The powdered gum-resins should never be used. The whole gum-resins are easiest powdered in small quantities by thoroughly chilling and rubbing in a *cold* mortar.

CLASS III.—OILS, OLEO-RESINS, AND HYDROCARBONS

This class includes the liquid balsams, and all liquid bodies which do not admit of evaporation, and therefore require to be solidified by absorption, or in some other manner. They are the most troublesome of all the pill ingredients to form into *small* pills. Were the size of the resulting pills of no importance they could be easily managed, but the inexorable rule to "make the smallest pill possible" (down to one-half grain), demands, oftentimes, seeming impossibilities. The selection of the excipient which will yield the smallest pill, together with a proper mass, is no light task. Thin liquids are more troublesome than viscid, and volatile oils more than fixed.

Magnesia is the most efficient excipient and the most objectionable, and should never be used except as a last resort. When used, time should be allowed for it to set, and this may be hastened by applying a little heat.

Failure sometimes results with it, owing to the fact that no aqueous moisture is present, and it is always safe to sprinkle a few drops of water upon it before incorporating with the oil or other liquid.

It has been claimed that lanolin will prevent a magnesia mass from becoming very hard, if used to the extent of 1/12 the total weight of the mass.

Wax comes next in efficiency, and is less objectionable, particularly when used in combination with starch or some vegetable powder.

From half to an equal weight of wax is needed for oils and other fluids, according to the viscosity.

Sometimes a little tragacanth or extract of licorice is needed to make the mass more adhesive.

The mixture of wax and flour, with which the liquid may be incorporated by trituration, usually makes a good mass. When the mass is made by mixing the liquid with melted wax, it is well to chill the mixture afterward, remembering that a freshly congealed fat or wax is never as firm as one which has stood for some time in a cool place. It is well also to add only half the liquid to the melted wax at first, and after incorporating this the remainder may be incorporated also. In this way lumping, caused by the too sudden cooling of the wax, is avoided. Such lumps are hard to eradicate.

Cacao butter has been recommended as a substitute for wax, but pills made with it must be kept in a cool place.

The trouble with employing wax or cacao butter for extemporaneous preparations of pills is that time is required for the mixture to set, and if the wax is used in small proportions, unless several hours can be allowed for the mixture to stiffen, the pills are likely to be too hard to disintegrate in the stomach. The mixture of wax and oil should be chilled, as in suppository-making, before the mass is made up, to avoid this.

Thin and mobile fluids do not mass as well with these as viscid bodies, and with thin liquids a smaller pill may be made by use of flour or althæa and syrup, than with wax.

Soap makes an excellent excipient for the fixed oils and balsams or oleoresins, but is less efficient with volatile oils and the hydrocarbons. When used in a mass containing an oil and solid bodies, it should be first mixed with the oil alone, then this mixture added to the other ingredients.

When added to the entire mass the results are not as good. In all masses containing both liquids and solids, the first aim should be to get the liquid into suitable condition, and while allowing for the absorptive or solidifying powers of the other ingredients, the attention is first devoted to the massing of the liquid.

Absorbent powders are often preferred when so much is not required as to make an unduly large pill. A mixture of two parts of licorice root with one of licorice extract has considerable binding as well as absorptive powers. This makes a good mass where not more than one minim of liquid is to be contained in a pill. Sometimes other vegetable powders are used when they agree with the medicinal action of the pills. Flour and althea are the best of the white absorbent powders. Kaolin is also good. All of these require some aqueous fluid to develop their adhesiveness, which should be added.

An ingenious method for making liquid bodies into pills has been proposed by Mr. William Kerchumann, who suggests to make first an emulsion with acacia, to which is added magnesia, and after standing twelve hours borax is added to coagulate the gum and make a mass.

This is interesting from the principles which it involves, but is open to the usual objections to magnesia and alkalies as excipients.

Another method which is particularly convenient for massing volatile oils, etc., which are frequently ordered in pill form, is to keep in stock a jelly containing a definite proportion of oil, and making the mass from this with licorice or althæa.

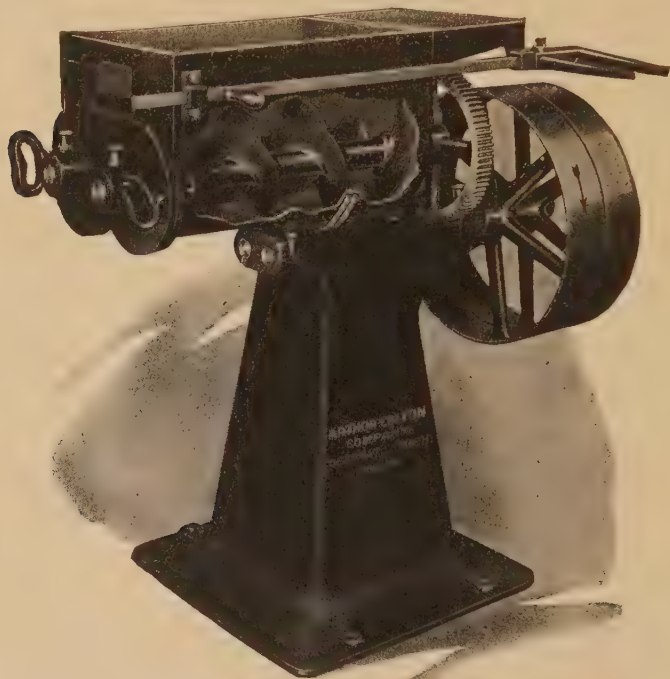


FIG. 18.—Worm massing machine.

A paste made from 5.5 parts of gelatin, 2.5 parts of sugar and 12 parts of water, will gelatinize an equal weight (20 parts) of creosote, phenol or an oil, and if preserved in a bottle covered with a layer of diluted alcohol, will keep almost indefinitely. Two parts of this jelly are used for each part of oil or creosote ordered, and a mass is quickly made by incorporating a sufficient quantity of licorice or althæa powder.

CLASS IV.—CHEMICAL BODIES

These are of two kinds, the organic chemicals and the inorganic. They require much judgment and a knowledge of chemical reactions and compatibilities. When crystalline bodies are to be incorporated in pills, they should first be finely powdered, and in case of powerful

remedies it is advantageous to dissolve them in water or glycerin, and add this solution to the mixture, taking care that no more liquid is used than will make a good mass.

In this way the crystalline structure is destroyed, and the potent remedy thoroughly diffused through the mass with a minimum of labor.

The oxidizing agents, as permanganate of potassium, silver salts and the salts of mercury, require special precautions, which are treated under their separate heads.

ORGANIC CHEMICALS.—The most important of these in pill-making are the alkaloids.

When the **powerful alkaloids** are to be massed, such as strychnine, atropine, etc., special care should be exercised in weighing and mixing them. The safest and quickest way of mixing them is either to add them to the other ingredients in solution, as already suggested, or to mix first with an equal bulk of another powdered ingredient, which mixture is then diluted with the remainder, gradually added, so that a uniform admixture is assured. Pills of these should be made to weigh about one-half grain each, some inert body like starch or licorice being used as a diluent when needed.

Quinine pills are perhaps the most common of the alkaloidal pills, the sulphate being generally used. No difficulty is found in massing quinine with the usual liquid excipients, glucose, glycerin, mucilage or glycerite of tragacanth, etc., all giving a plastic and adhesive mass. If a white pill is desired, only a white or colorless excipient may be used, and the most scrupulous cleanliness observed, both with the hands and the utensils. Even then a very free use of starch as a dusting powder is usually necessary.

The use of acids as excipients for these has often been suggested, the purpose being to obtain smaller pills. Tartaric acid, in the proportion of one grain to six to ten grains of the quinine, citric acid in about the same proportions, lactic acid and dilute mineral acids in quantities sufficient to mass, are usually recommended. These all make a mass which is very plastic and easy to work at first, but which loses its plasticity very rapidly and becomes hard and immobile.

Rapid work is required, both in massing and rolling these, in order to finish the pills before the mass has set.

Synthetic Remedies.—These are mostly organic, and include such bodies as antipyrine, acetanilid, salol, etc.

The choice of an excipient for these depends almost entirely upon their solubilities.

Those soluble in water may be massed with glucose, mucilage or glycerite of tragacanth, honey, etc. These would also make a good mass with many which are very slightly soluble in water.

Such as are insoluble in water may be massed with glycerin, or a viscid oil, either with or without soap—preferably with.

The adhesive excipients may also be used with these, but will make a larger pill, in most cases.

Camphor, Phenol, Thymol, Chloral, etc.—These make little trouble when massed alone, but when mixed together or with resinous bodies they partially or completely liquefy. When this takes place, the liquid is best absorbed by means of flour or licorice, and massed with syrup or glucose.

When partial liquefaction occurs, the mass may often be made by simply beating the ingredients together in a warm mortar, without the use of any incipient. In such cases alcohol or ether should not be used to powder the camphor, lest the mass be too soft.

If it is necessary to powder the camphor a little chloroform may be used, and then after triturating the camphor to a powder the latter should be thoroughly dried before mixing with the other ingredients.

Soap with oil or water makes a good excipient for these when needed. Phenol, chloral, etc., may also be massed with althæa and glucose, or licorice and mucilage of tragacanth.

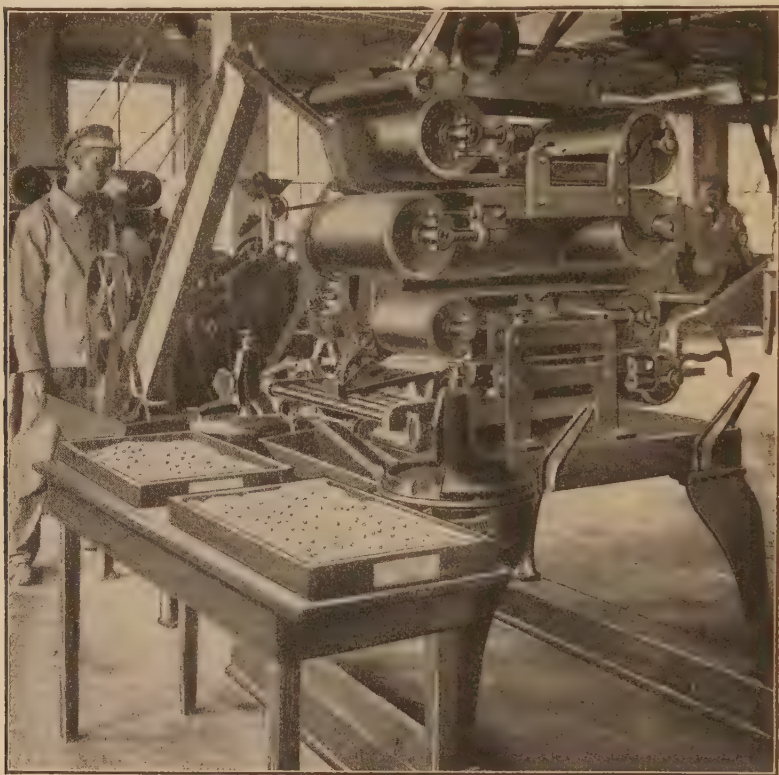


FIG. 19.—Automatic pill machine. Capacity 100,000 pills per hour.

Glyceryl tritnitrate (nitroglycerin) requires especial care in handling. It is quickly absorbed through the skin and produces a bad headache which lasts for some hours. **Rubber gloves should be worn** when making pills containing this substance. It explodes readily when triturated dry, but the presence of enough moisture to form a pill mass will prevent this.

Other organic bodies are treated according to their general characteristics. Organic acids mass well with glycerin, but when the acid is very soluble in the glycerin, as tannic acid, the pills must be finished quickly, because the mass soon hardens.

Glycerin forms a good general excipient for many organic bodies.

INORGANIC CHEMICALS.—Iron and mercury and their salts are most frequently prescribed in pills, but certain salts of potassium and silver are also used, and occasionally the salts of the other metals. Most salts require the addition of a vegetable powder to make an adhesive mass, and in the case of hygroscopic or deliquescent salts, to also absorb the moisture in the excipient and air, which would otherwise soften or liquefy the salts on standing. Powdered licorice-root or extract, or althaea are best to use for this purpose in the absence of any other vegetable constituents of a mass. Sugar is employed in the iron pills, and acts both as a binding and a protecting agent.

Very deliquescent salts, like potassium acetate, seldom ordered in pill form, require to be massed with a moisture-repelling excipient. Canada balsam, cacao butter, resin cerate, or hard petrolatum answer well for this purpose.

If the salts are crystalline they should first be very finely powdered, then mixed with the vegetable powder or with extracts.

Glycerin should not be used for massing metallic oxides or basic salts, because it forms a hard, stone-like cement with many of these. In general, glycerin is a poor excipient for metallic salts or bodies, though it may be used in some cases.

Soap is incompatible with all the metallic salts except the salts of potassium and sodium, forming insoluble metallic soaps, hence it should never be used in masses containing these.

Iron and iron salts are much used in pill-form, and offer some peculiar difficulties. There are three classes of these: (a) Those containing metallic iron or ferrous salts; (b) those in which a reaction occurs in making the mass; (c) those which contain ferric salts.

(a) When metallic iron, as reduced or "alcoholized" iron, is made into pills a good binding agent is needed, and since this is a heavy powder a bulky excipient is often to be preferred. Extract of licorice (one to ten) and glucose, or manna and syrup, make an excellent mass. Confection of rose or mucilage of tragacanth are also good excipients.

When **ferrous sulphate** is to be made into pills the dried salt, Ferri Sulphas Exsiccatus, U. S. P., may be used. This makes a better and less changeable mass than the crystals.

If the crystals are ordered, the dried salt may be substituted in the proportion of three grains of dried sulphate for each five grains of the crystals. This should not be done, however, if the pills belong to class b.

Ferrous sulphate may be massed in the same manner as reduced iron.

(b) **Ferrous carbonate** is a very desirable form of iron, but cannot be kept in a dry condition, unless protected, and hence is obtained for pills by a reaction which takes place between crystallized ferrous sulphate and sodium or potassium carbonate in making the mass.

In making masses of this character only the best materials should be used, since a ferrous sulphate which is slightly oxidized will not yield a bright-green ferrous carbonate, and the mass should be exposed to the air as little as possible to prevent oxidation after the carbonate is formed. When these precautions are taken a bright-green mass, the color of true ferrous carbonate, results, but with an impure ferrous

sulphate, or with an undue exposure to air, the mass is darker, and may be almost black.

Two forms of this are official—Vallet's mass, *Massa Ferri Carbonatis*, and Blaud's pills, *Pilula Ferri Carbonatis*—the difference between the two being that in the first case the alkaline sulphate, which is formed by the reaction, is removed by washing, while in the second case it remains as an ingredient of the pills.

In making Vallet's mass, solutions of ferrous sulphate and sodium carbonate are mixed while hot, and the resulting precipitate of ferrous carbonate is washed with distilled water, which has been boiled to expel all dissolved air and mixed with syrup to further protect the precipitate from change, until the sodium sulphate is removed, then the precipitate is quickly drained in a covered funnel and added to a mixture of honey and sugar and evaporated to a pilular consistence. It is during this draining and evaporation that the greatest change takes place, and great care is required to obtain a greenish mass—it often becoming black.

The process is rendered easier if the salts are mixed while the solutions are hot, in order to get a more dense precipitate, which is then washed by a hot saccharine solution instead of cold, and finally the drained precipitate mixed with the sugar and added to the honey which has previously been evaporated to half or two-thirds its original bulk. By this means the evaporation of the mass is much hastened and the salt is exposed much less.

In the Blaud's pill, crystallized sulphate of iron is used because this dissolves much more quickly and consequently reacts more promptly than the dried sulphate. The mass is made by moistening the potassium carbonate with glycerin and water, then adding the ferrous sulphate mixed with sugar, which is used to protect the ferrous carbonate which is formed, and beating into a mass, which rapidly becomes a deep green. The tragacanth and althea are then incorporated and the mass divided into pills. During the reaction water is liberated from the ferrous sulphate, which aids the reaction and also softens the mass. Potassium bicarbonate should never be used in making these or similar pills, because carbonic acid gas and water will be given off during the reaction, causing the mass to swell. The mass must then be allowed to stand for some time until the reaction is complete, making an undue exposure, or if rolled into pills quickly these are liable to be forced apart by the escaping gas.

Pills of iodide of iron are another instance of a reactionary mass, the iodide of iron in this case being formed by direct union of reduced iron and iodine in contact with water. An excess of iron is used because the salt is less easily decomposed or changed in the presence of metallic iron, and sugar is also added as a further protective. The mass (the other ingredients having been added) is then evaporated on a water-bath, with constant stirring, and finally divided into pills which are then varnished with tolu to prevent all access of air. It is much easier to get a satisfactory mass of iodide of iron than one of carbonate of iron, regarding the final condition of the ferrous salt.

The finished pills each contain a trifle less than one grain of ferrous iodide and one-half grain of reduced iron.

(c) **The ferric salts** which are used in pills are mostly the oxide, hydrated oxide, soluble oxide, or the scale salts, as the citrate, phosphate, etc. The oxide and hydrated oxide are seldom used and present no difficulties, requiring simply an adhesive excipient.

The soluble oxide (saccharated oxide of iron or *Eisenzucker*) and the scale salts are quite soluble and care must be taken not to add too much excipient. It should be remembered that there are two forms of citrate of iron, one designed for pills, which is very soluble, but slowly so, and the ammonio-citrate or "soluble citrate," which is quickly soluble.

The latter is not well adapted to massing, though a good pill can be made from it with glucose or syrup if used cautiously. A single grain too much of excipient in a small mass will, however, change a firm mass into a semi-liquid paste. Similar results will follow in massing the soluble oxide and the citrate of iron if too much excipient be used, though not as easily. Masses made with aqueous excipients are also hygroscopic, and require to be kept from contact with the air either by coating or by storing the pills in tight containers, with an excess of licorice powder, etc.

For these reasons the fatty excipients, as *petrolatum*, simple ointment, Canada balsam, cacao butter, etc., are recommended for making these pills, a slight excess having no solvent action upon the salt and therefore doing no harm, and the pills are not hygroscopic. These excipients do not make as firm and plastic a mass as glucose, mucilage of *tragacanth*, etc., but are otherwise unobjectionable.

Mercury and Mercury Salts.—Pills containing metallic mercury are made by first emulsifying the mercury with some viscid body in order to finely subdivide it, a mixture of honey of rose and the oleate being used in the official process. The dense emulsion is then stiffened into a mass by incorporating inert powders, licorice and *althea* being used for that purpose. This forms an excellent mass, but it must not be triturated or worked very much or the mercury will separate and collect on the surface in little globules which cannot be reincorporated. The same is true of other preparations containing finely divided mercury, as mercury with chalk; a good mass may be obtained by use of mucilage of *tragacanth*, but the mass must not be worked any more than is really necessary lest the mercury separate.

Mass of mercury (blue mass) is often incorporated with other cathartics and extracts.

It is best triturated first with the dry powders, then excipient (glucose, honey or glycerin) is added and the mass rolled. The mercury is more liable to separate from a mass than from dry powders.

Mercury salts need to be handled very carefully in order to avoid reduction. Contact with metals, even as slight as in the use of a steel spatula or the cutting of the mass upon the brass plates of a pill-machine, is sufficient to reduce many of the salts of mercury when moist; consequently these should not be used for masses containing mercury salts. The mass should be worked in a wedge-wood mortar, using a horn or rubber spatula, and the pipe cut upon a rubber machine or a pill-tile.

An illustration of the ease with which mercury salts are reduced occurred in a manufacturing establishment some years ago, when

calomel pills, made with starch and glucose as excipients, unaccountably lost their bright, white appearance and became gray. Acting upon the supposition that this was due to carelessness in working or handling the mass, another lot of several thousand was made, using great care in selecting the materials and working the mass. These darkened in the same manner after standing a few days. An investigation was then made, and the trouble found due to minute traces of iron in the starch from the iron mills in which it was ground. Starch ground in burr-stone mills was obtained, and calomel pills made with this remained white.

Some of the mercury salts are also reduced by rubbing, particularly when dry, and it is always wise to moisten them with a little water or excipient before incorporating them with intractable bodies, to avoid any possibility of reduction. If they are to be mixed with a powder, as starch, licorice, etc., the moistening is unnecessary, but the powders should be triturated very lightly.

Probably the best excipient for these pills, when they are to be dispensed without coating, is that proposed by Mr. Thomas Wiegand—a glycerite of tragacanth, made by triturating 4 Gm. of powdered tragacanth with 96 Gm. of glycerin, and allowing to stand over night.

In place of this, glycerite or mucilage of tragacanth may be used. Glucose is said to reduce pills of calomel, but probably much depends upon the glucose in question, since pills made with this have shown no sign of change on keeping. Manna has been highly recommended for massing these, and may be used without the addition of a vegetable powder.

Glucose is liable to contain a trace of sulphite, due to sulphurous acid used in bleaching it. This may account for reducing actions.

Phosphorus Pills.—When phosphorus is to be incorporated in pills, it should always be added to vegetable powders in solution.

The best solvents for this purpose are chloroform and carbon disulphide. Special precautions must be observed in weighing the phosphorus, since it begins to oxidize as soon as it is exposed to the air, if dry. It should be weighed under water, and care be taken that water is not weighed as phosphorus nor phosphorus as water. In order to avoid these errors, a capsule or watch-glass containing a little water is first counterpoised upon the balance; then a piece of phosphorus of the judged size (which has been cut under water in another dish, then dried by pressing in dry filter-paper) is dropped into it and weighed. If too heavy, it is removed from the water, the capsule and its contents again counterpoised (for in taking out the bit of phosphorus enough weighed water will have been removed to make a serious error in the ultimate weight of phosphorus, unless corrected), then a smaller piece is dried, dropped into the water and weighed as before. This operation must be repeated until the desired weight of phosphorus is obtained.

The weighed phosphorus must then be thoroughly dried with filter-paper or absorbent cotton, before dropping into the solvent, for a little moisture may hinder solution.

The solution should always be made in a small (homœopathic) vial or test-tube, selecting one, if possible, which will just hold the liquid without leaving much air space.

If free contact of air is allowed while the solution is taking place, part of the solvent may be lost; and what is worse, the phosphorus will be partially oxidized, and then a clear solution cannot be obtained.

This will also occur if the liquid be violently agitated in a vial or tube which it only half fills.

The solution having been obtained, it is then poured upon the dry powder in the mortar, stirred lightly to moisten the powder evenly, and also to favor evaporation, but avoiding the spreading of the paste about the sides of the mortar; and when the liquid has nearly evaporated and fumes begin to come off, the liquid excipient (glycerin, glucose, syrup, etc.) should be added and incorporated as quickly as possible. All the liquid excipient should be added at once when the amount needed is known. The aqueous excipient will prevent further oxidation of the phosphorus, but the pills should be coated with tolu as soon as finished.

When phosphorus is prescribed alone in pills, licorice, althea, flour, starch, or any inert powder may be used for absorbing the solution. When other powders enter into the composition of the pill these will serve the same purpose, extracts or fluids being added last.

Phosphorus pills have been made by dissolving the phosphorus in hot cacao butter, and when the fat has solidified, rolling it into pills. They are then dusted with desiccated chocolate and sugar to cover the odor and taste. Wax and resin have also been used in a similar way.

The *British Pharmacopæia* directs a phosphorus mass to be made by triturating 3 grains of phosphorus with 120 grains of tolu balsam under hot water until no particles of phosphorus are visible. Then 57 grains of wax are added and thoroughly incorporated, also under water.

The water must be kept hot enough (60° C. or above) to melt the phosphorus and thoroughly soften the balsam and the wax, and the mass so made is stored under cold water. When dispensed every two grains, representing $\frac{1}{30}$ grain of phosphorus, are incorporated with one grain of powdered curd soap, a little alcohol being used if necessary to obtain a plastic mass, then rolled into pills.

Silver Salts.—These are all reduced by contact with vegetable matter, and form an exception to the general rule that inorganic salts should be mixed with a vegetable powder.

To do so with the salts of silver would result in a complete reduction of the salt. This is also brought about by the ordinary excipients, and these too should be avoided.

Since the salts of silver are heavy bodies and are given only in small doses, some diluent is necessary, and an inert inorganic body should be chosen. Kaolin (china clay), talcum, or Fuller's earth are best for these.

A mixture of silver oxide or nitrate with kaolin or Fuller's earth masses well with water, but the pills are apt to crumble when they become dry. Coating with tolu retards this.

A better mass is obtained with hard petrolatum (or a mixture of petrolatum and paraffin about the consistence of ointment) or resin cerate.

These are organic bodies, but having no solvent action upon the silver salts, the latter are only slightly reduced, particularly by petrolatum. Pills made in this way have shown scarcely any change of the silver salt after keeping several years.

Anhydrous sodium sulphate and kaolin, in the proportion of one part of the dried sodium sulphate to two of kaolin, massed with one of water has also been recommended for such pills. The silver salt is mixed with this and then made into a mass which must be rolled quickly, as it soon becomes brittle.

The water enables the sodium salt to crystallize, and it sets into a hard strong mass like plaster of Paris, which is readily soluble in water. The mass remains plastic only about 5 to 10 minutes, and must be worked before it begins to harden.

The British Pharmaceutical Codex gives the following combination as an excipient for this class of pills.

Kaolin, in fine powder.....	25
White Petrolatum.....	50
Paraffin.....	25

Mix as for an ointment.

This makes a good excipient for most of the reducible organic salts.

Occasionally silver nitrate or oxide is ordered combined with an organic body in pills, as pills of silver oxide and creosote. If these are mixed directly an explosion (in this case) will occur. The only way to prevent this is to make a small mass of the silver oxide with kaolin and petrolatum, also a mass of creosote with wax, flour and water, then mix the two masses and roll. Even then a reaction is liable to ensue.

Potassium permanganate reacts with organic matter and is reduced, consequently it should always be massed with clay or talcum and petrolatum and rolled on a glass tile or rubber pill-machine. All that has been said regarding the massing of silver salts applies to this also. The best excipient is kaolin and hard petrolatum.

Other Salts.—Occasionally some of the salts of arsenic, calcium, copper, lead, potassium, sodium, zinc, etc., are ordered in pill-form. These offer no difficulties beyond the special ones already mentioned under the general head of inorganic chemicals.

It should be borne in mind that salts of bismuth and copper are reduced by prolonged contact with iron, and these should not be massed in an iron mortar, nor with a steel spatula upon a tile. The soluble salts may be mixed with licorice, althea, etc., and massed with glucose, and the insoluble salts are massed with extract of licorice or mucilage of tragacanth.

This latter contains some glycerin, but not enough to exercise a very decided solvent action.

PILL COATINGS

Pills are coated to cover the taste, to prevent change by excluding air, and to render them more slowly soluble, or even insoluble in the stomach. In the latter case the pills are intended to pass through the stomach entire and dissolve in the intestines.

The coating of pills is an art which demands considerable practice, and the knack for which is less readily acquired than for most pharmaceutical operations.

The pills must be made firm and the use of hygroscopic excipients should be avoided. The latter are apt to attract moisture from the coating and cause it to crack. When gelatin is used over a glycerin excipient the coating is likely to soften.

On the other hand, the pills should be dry enough, so that moisture will not exude and the coating become softened or dissolved. It is customary for the manufacturers to dry the pills in a warm place for a number of hours before coating.

The surface of the pill is thus hardened while the interior still remains soft.

Coated pills are almost always more slowly soluble than uncoated, but the solubility should not be hindered to any great extent.

Dusting powder should be thoroughly removed before coating, particularly when a transparent coating is to be applied.

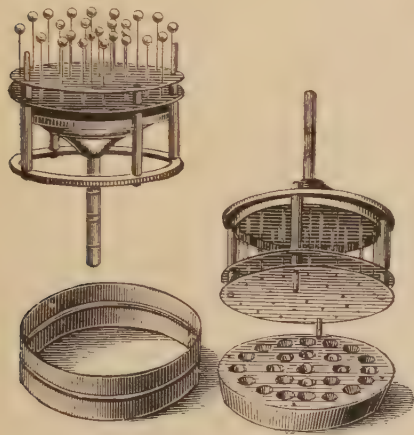


FIG. 20.—Maynard gelatin pill coater.

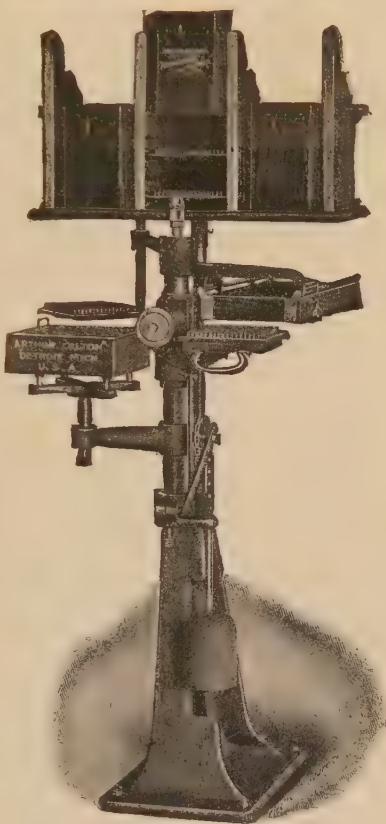


FIG. 21.—Gelatin coating machine.

This is best done before the pills are made, *i. e.*, by making the mass so firm that no conspergent is needed. If necessary to use it, licorice is commonly better than lycopodium, as it colors the pills more evenly.

It may be removed by shaking the pills in a sieve. If the surface of the pills still presents a variegated appearance, do not apply the coating at once, but either remove all of the objectionable powder with a brush, or cover it and the pills with a little moist lamp-black (or starch), so that the color will be uniform when coated. If an opaque coating is to be applied, this is not necessary.

Varnishing is the term sometimes applied to coating with resinous or balsamic substances, as tolu, mastic and the like. The ordinary varnish, such as is used for wood-work, is never used, but an ethereal solution of tolu, etc., constitutes the varnishing agent.

These coatings are specially adapted for dispensing exigencies, and are often directed for pills which are liable to change on exposure to air. Tolu coating is directed to be used on the phosphorus and iodide of iron pills as a protective.

An old tolu, which has lost much of its oil and become brittle, is better for this than a fresh balsam.

The resinous remainder of tolu which has been used in making syrup of tolu by the former (1880) official process, or tolu which has been well washed in hot water, may be used in place of fresh tolu.

The tolu having been dissolved in ether, a few drops are placed in a capsule and the pills rotated in this until uniformly coated and the ether has evaporated.

If a strong solution is employed, as directed by the Pharmacopœia, only a few drops of solution should be used at a time, commonly about half as many drops of solution as there are pills to be coated.

Novices are prone to use a large quantity of the solution, whereby the pills are wetted more quickly, but on evaporation of the ether the pills will become sticky and adhere to everything they touch. If this occurs the best treatment, after separation of the pills, is to place the container on ice in order to harden the coating. It can be obviated by using only a few drops of the solution at a time, and repeating the operation until a sufficient coating has been obtained, or by using a more dilute ethereal solution. A thick coating must not be expected, only enough being needed to form a thin film of resin around the pill.

A still better way of applying the coating is to spray the solution upon the pills from an atomizer, keeping the pills constantly in motion.

Combinations of tolu with other bodies are used, as tolu and sandarac, tolu and mastic, etc. These make a harder coating than tolu alone, and are also more easily applied.

Three parts of tolu and seven parts of mastic or sandarac dissolved in ether or absolute alcohol make a good solution. Ether volatilizes more quickly than alcohol and is preferable on that account.

When the pills are to be double coated, and sugar or gold leaf is to cover the varnish, special treatment may be required to enable the second coating to adhere to the resinous one.

If sugar is to be applied by intervention of mucilage the gum will not adhere to the resin unless the latter be first moistened with a little weak solution of potassa, whereby the resinous coating is partially saponified. When heat is used, this is unnecessary.

SUGAR AND PEARL COATING.—Sugar coating is probably the most common of the commercial coatings. It requires more practice to obtain satisfactory results upon a small scale than other coatings, and the best results can only be obtained by operating upon a quantity of pills and by means of expensive apparatus. Sucrose alone is never used for coating, being too translucent, but is mixed with some fine, insoluble, white powder, as starch, arrow-root, talcum, etc. or lactose.

A good mixture for use at the dispensing counter is milk sugar, 6 parts; starch, 1 part; and powdered acacia, 1 part. To coat pills

with this, moisten them first with a little water or syrup, and place in a round box or coating-sphere with some of the coating mixture, using about a teaspoonful of the mixture to each dozen pills. Roll the pills thoroughly in the powder, then transfer them to a clean box or sphere and polish them by attrition. If the first coating is not heavy enough the process must be repeated.

On the large scale the pills are not moistened, but, having been partially dried, are placed in a pear-shaped vessel made of copper,

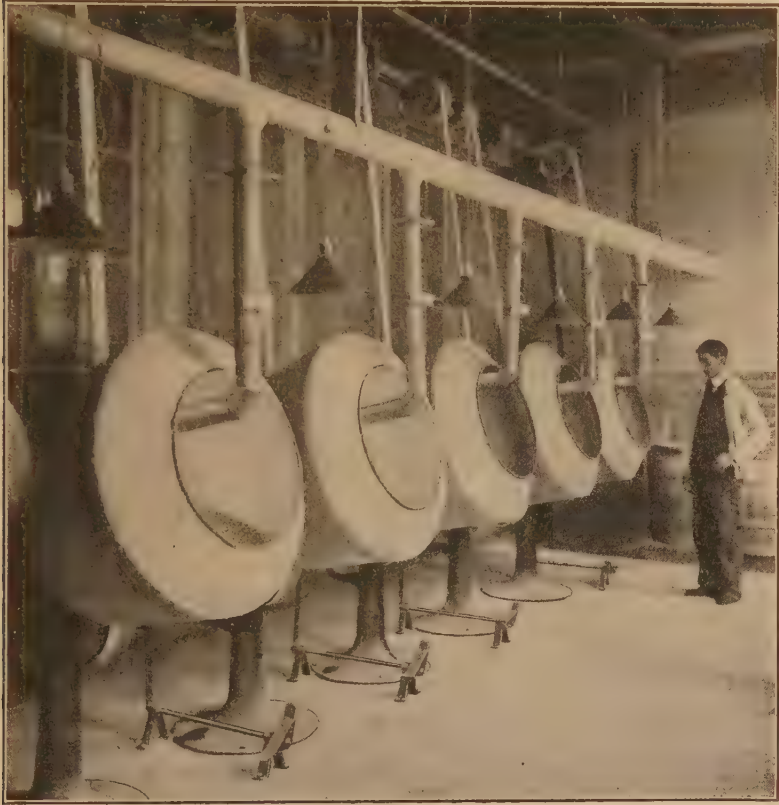


FIG. 22.—Pans for sugar coating pills and tablets.

which is mounted on the end of an oblique shaft, and is surrounded by a steam coil or jacket so that the vessel may be heated. A gentle blast of warm air is also blown upon the pills or tablets as they are being rotated.

The necessary quantity of sugar mixture is then added, and the closed vessel is made to revolve. Steam is now turned on, and the vessel is heated just enough to partially melt the sugar and make it sticky.

When the coating has been evenly distributed over the pills the steam is shut off and the revolving continued until the pills are pol-

ished and the coating is hard. A smooth, glossy coating of any desired thickness is obtained in this way, which is impossible by hand methods.

It is possible to make pills in a similar manner by using medicinal agents in place of the sugar mixture. A minute pill or nucleus is first made in the usual way, say of quinine, then these nuclei are placed in the coating apparatus and coated with quinine until a pill of the desired size is obtained.

Such are called *aggregation pills*, or *friable pills*.

These may afterward be coated with gelatin or sugar, etc. Such a process is of questionable value when medicinal agents which are injured by heat are so treated, but has the advantage of yielding a pill which is easily disintegrated.

Pearl coating is similar to sugar coating, but contains a large proportion of powdered soapstone or talcum, so that the pills have a pearly appearance.

Sometimes talcum alone is used. The coating is applied in the same manner as sugar coating.

In moistening the pills with mucilage do not apply enough to give them a wet and shiny appearance; only two or three drops of liquid are necessary for each dozen of pills. The easiest way of applying it is by spraying from an atomizer. If the gum is mixed with the coating powder the pills are readily moistened in a sieve by holding them for a moment in the steam arising from boiling water.

Egg albumin and gelatin are also used for moistening previously to rolling in the powder. The former is easily applied and gives good results, being prevented from subsequent change by the preservative powers of the sugar, and also by drying. Gelatin is less easily applied and offers no advantages. If used, the vessels and the solution must be warm.

These require more time in hardening than when mucilage or albumin is used.

Chocolate coating is similar to sugar coating. It consists of a mixture of fat-free cocoa and sucrose, and is best applied as a syrup. A dry mixture of cocoa and sugar, applied by the method described under sugar coating does not make an even and smooth surface on the pills, and the color will also vary. To secure a dark and smooth coating a strong syrup is prepared and this is poured, while warm, on the pills in a coating pan. The warm air evaporates the water, while the constant rotation distributes the coating evenly. Several applications are necessary to obtain a sufficient thickness of coating. An under coating which is usually colored with iron oxide protects the pills from solvent action by the warm syrup, and also forms a ground for the color, which is of advantage.

GOLD AND SILVER COATING.—This form of coating is very old, but is not now used as much as formerly except for cachous. Gold and silver leaf are used, the pills being first moistened with a little weak mucilage (care being taken not to use too much), then shaken with the leaf. The shaking must be continued for some time, and a second coating is often necessary to give a bright and smooth appearance, and entirely conceal the color of the pill mass. Albuminum leaf may be used in place of silver leaf for the first coating. Being after-

ward covered with silver, the pills are just as bright and the cost of materials is less.

This is one of the easiest forms of coating to apply, and is readily employed at the dispensing counter. But the pills must be not too wet or the coating will not cover the pills well, and will be dull and irregular. One leaf of silver or gold is sufficient to coat six to a dozen pills, according to size. If the pills contain any sulphides they must first be coated with tolu or sandarac to prevent the discoloration of the silver after-coating. Gold leaf is much better for these.

If a bright surface is not obtained, after the pills are well covered with the leaf, they should be moistened (not wetted) with alcohol and again shaken with a little fresh leaf. This will usually produce a polished surface.

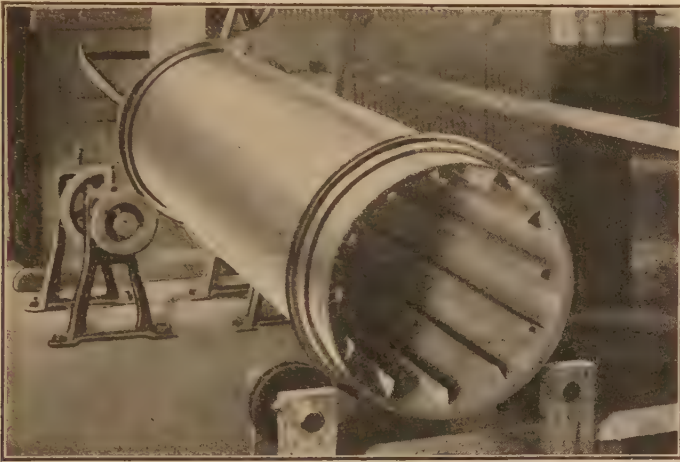


FIG. 23.—Drum for removing powder from pills before coating.

GELATIN COATING is a less common form of coating than formerly. It is attractive in appearance, practically tasteless, and is readily dissolved in the stomach. Pills which are to be gelatin-coated should be firm, but not too hard, and should contain no glycerin.

The pills are partially dried before coating, so as to form a crust on the surface of the pills upon which the gelatin sets.

It is not so well adapted to the pan method of coating—which is the most economical method—hence it has been largely superseded by sugar and chocolate coating.

The gelatin shrinks on cooling and presses upon the contents of the pill, and, unless the mass is firm enough to withstand the pressure, some of the interior of the mass may be forced out through the pin-hole of the coating.

Pills are frequently covered by an inert powder before coating, in order to present a brighter and more even appearance. This is particularly true of black pills which are shaken just before coating in a little moist lamp-black, so that the finished pills are jet black and glossy, though the mass may have been grayish- or brownish-black.

In order to judge of the color of a coated pill it is necessary to cut or break it open and observe the interior of the mass.

Pills which are not readily soluble in aqueous solutions, as quinine pills, reduced iron, etc., and which are non-resinous in character, are easily coated with gelatin, and, after a little practice, may be satisfactorily done at the store, but the coating of all kinds of pills calls for much skill and experience.

The behavior of the coating varies with pills of different character, and the consistence and temperature of the gelatin solution into which the pills are dipped are matters of importance. In general, a hot and thin solution gives the best coating, but if resinous pills are dipped into such, the resins will be softened by the heat and the pills are likely to spurt. Likewise, with very soluble ingredients, as sodium salicylate, the momentary contact of the pill with the hot liquid is enough to partially liquefy the surface of the pill and the shape is spoiled. Such pills need to be dipped in a solution which is kept as cool as possible.

The scum which rises upon the surface of the gelatin solution must be brushed aside each time, and the pills dipped only into a clear solution, or air bubbles or other irregularities will show themselves upon the surface of the pill.

The solution should always be heated by steam or a water-bath, as it is quite likely to burn if direct heat be applied.

Various formulas for the coating solution are in use, some being secret and carefully guarded by the manufacturers. Professor Patch's formula gives good results. Best French gold-labelled gelatin, 2 1/2 ounces avoirdupois; distilled water, 7 fluidounces. Digest the gelatin in the water until a clear solution is obtained, then add 1/2 ounce of sugar, 2 drachms of powdered boric acid, and slowly, 2 fluidounces of mucilage of acacia, U. S. P.

Strain into suitable containers and allow to solidify. This forms a dense stock-jelly, which needs to be diluted with water when used for coating.

Only the best white gelatin and white gum acacia should be used, particularly for white pills. Even with dark-colored pills a much handsomer coating is secured when clean and white materials are used.

The hot solution should be kept covered while in use to prevent loss of water by evaporation. It should also be stirred each time the pills are dipped to keep it of uniform consistence. Never use a solution into which dark-colored pills have been dipped for coating white pills.

The older method of coating with gelatin is by impaling the pills upon the points of needles, the latter being set into a suitable frame so that a number of pills may be impaled and dipped at once. Several machines are in the market suitable for use on a small scale, one of the best being Professor Patch's machine. Full directions for use are given with each machine, so that these are unnecessary here.

In an emergency a few pills may be coated by sticking a dozen or more needles through a specie cork, the pills then being impaled upon the ends of the needles and dipped into the solution.

The cork with its load is now kept in irregular motion to prevent the coating solution from flowing to one side of the pills, until the solution has set, and after being allowed to stand until the coating is hard they may be removed from the needles. Another method, much

less satisfactory, is to place a few drops of the solution in a warm capsule, and roll the pills in this in the same manner as coating with tolu. Care must be taken not to use too much of the solution, and not to have the capsule too warm.

The needle method is open to the objections that a minute hole is left in the pill and the coating, through which some of the mass may be forced by the contraction of the coating; a little spur of coating also remains when the needle is removed, caused by the coating which adhered to the surface of the needle above the pill. The spur is removed by attrition or by cutting with small curved scissors.



FIG. 24.—Gelatin pill coater. Vacuum method.

In order to obviate these objections there are in use machines in which the needles are replaced by minute tubes terminating in a little cup which is not large enough to cover the pill. A series of such tubes are connected through a common bar-tube with an air-pump.

The pills having been placed in suitable sockets are covered with these little cups, the air sucked out of the apparatus and the pills are held upon the cups by air-pressure. The external portion of the pill is then dipped into the solution, and when dry the pills are reversed and the uncoated portion dipped. In this way a smooth coating is obtained in which there are no holes. Such an apparatus is too complicated and expensive for any except the largest manufacturers.

Gelatin coating is also applied by the pan method, the gelatin being mixed with some inert powder. This is the most economical method of coating, and is the process used by the larger manufacturers.

Most commercial pills have a series of three coatings to give them uniformity in color and general appearance. The first or subcoating is usually of gelatin because this both protects the pill mass from softening when other coats are applied, and it furnishes a surface to which other coatings adhere well. The second coat consists of insoluble and opaque powders upon which a final colored or white surface will reflect well. For white pills this second coating consists mainly of chalk, or Kaloin, and for chocolate-coated pills of ferric oxide mixed with Kaolin or chalk. The final coating is of sugar, either colored or uncolored, or of chocolate-sugar. Lastly a polish is imparted by rotating the pills in a pan the surface of which is coated with a thin layer of wax.

ENTERIC COATINGS

There is desired a special coating for pills intended to pass through the stomach unchanged and dissolve in the intestines. Such are (1) medicines which may irritate the mucous membrane of the stomach, such as arsenic, creosote, iron preparations, mercurial preparations, phosphorus and anthelmintics.

(2) Medicines which may hinder digestion by producing insoluble or inactive preparations with the gastric juice, such as tannin, alum, acetate of lead, corrosive sublimate, alkalies, sulphide of calcium, etc.

(3) Medicines which should arrive in the intestines in as concentrated form as possible, such as kousso, male fern preparations, santonin, etc., or which are decomposed in the stomach, as silver nitrate.

Pills so coated are sometimes called *enteric pills*.

The fluids of the stomach are usually acid in reaction while those of the intestines are alkaline, hence what is needed for an enteric coating is an impervious material which is insoluble in weak acids but soluble in weak alkalies. Such a substance is not easily found, for while there are many which will not dissolve in weak acids but will dissolve in weak alkalies, such as salol, yet the physical condition is quite as important as the solubility and an impervious as well as an acid-insoluble coating is needed.

Salol is the most common coating used for this purpose and the most frequently ordered. It is ideal in so far as its solubility goes, but it is a markedly crystalline body and it is difficult to make an impervious coating with salol alone. It is not applicable to pills of camphor, creosote, or other bodies which liquefy with salol, unless a protective coating intervenes. If the usual procedure be employed, to melt the salol in a capsule and roll the pills in the liquid until evenly coated, then allow it to harden, it will be found that upon congealing the salol crystallizes. The crystals will be smaller and the structure more compact if heat is used cautiously, only enough to melt the salol and warm the surface of the pills sufficiently to make it adhere. But at best the warm acid fluids will penetrate through the coating and disintegrate it, and when the pill swells the coating drops off without dissolving.

If the salol be dissolved in alcohol or ether and applied as a varnish, the results are similar but worse.

The best method is to combine the salol with a resinous or fatty body, which may form an impervious varnish-like coating, and yet

will not prevent the alkaline fluids of the intestines from acting upon the coating.

Tolu, colophony, stearin or tallow may be used. An ethereal solution is prepared containing enough of the resinous or fatty body to form a thin coating, then about one-half to one grain of salol is added for each pill to be coated and dissolved in the solution. The pills are then coated with this fluid, preferably on a pill-tiler or in an evaporating dish so that the ether will evaporate rapidly and the coating remain homogeneous.

The British Pharmaceutical Codex gives the following formula for a Salol Pill Varnish which makes satisfactory enteric coating when properly applied; salol 20 Gm., shellac 30 Gm., ether 30 cc. absolute alcohol to make 100 cc.

This is applied as a varnish to the pills, and the best results are obtained when several coats are applied in succession. But too thick a coating should be avoided because the shellac hinders solution in the intestines.

Care is needed to get a coating which is not too thick with resin, and so will dissolve very slowly in the intestines, and yet will be thick enough to protect the pill while it passes through the stomach. At best the coating with salol is of uncertain value, unless the operator is expert at it.

Keratin, a product obtained by digesting horn or bristles or feathers successively in ether, alcohol and dilute acids, has been recommended for enteric coating, and usually occupies a prominent place in pharmaceutical literature for this purpose. It is directed to be dissolved in weak ammonia water and applied, but it has been found that commercial keratin is either soluble in both acid and alkaline solutions, or else insoluble in either, hence it is useless as a coating. It may be dismissed as one of the delusions of the past.

Other agents that have been recommended are tannalbin, which like salol is insoluble in acids but soluble in alkalis; resins, particularly tolu, colophony, and shellac, and fats. An Italian pharmacist claims that mutton tallow will, when applied as a pill-coating, resist the stomach juices for an hour but will easily dissolve in the intestines.

Another recommends a combination of betanaphthol 6 parts, tannigen 10 parts and salol 20 parts dissolved in alcohol 30 parts and ether 100 parts.

Collodion has been suggested, but is of questionable value. It is more likely to cause the pill to pass through the entire alimentary tract without dissolving, than to make a true enteric coating.

This is the real danger of enteric coatings. If too resistant they do not dissolve at all, and if not resistant enough they have little value as enteric coatings. The really ideal coating for enteric purposes has not yet appeared, and the matter is still to be handled cautiously.

PILLS

- | | | | |
|----|------------------------------|--------|---|
| R. | Asafetida..... | 20 Gm. | . "Beat the solids together with water, so as to form a mass, and divide it into one hundred (100) pills."
Make 20 pills. These are best made in a slightly warm mortar. |
| | Soap, in fine powder..... | 6 Gm. | |
| | Water, a sufficient quantity | | |
| | to make one hundred pills. | | |
| M. | Sig.—Asafetida pills. | | |

11

- R. Potassii iodidi..... 2.00
 Olei theobromatis..... 2.00
 Petrolati..... q. s.
 M. Ft. pil. no xx. Sig.—“Iodide pills.”

12

- R. Mercury..... 33 Gm.
 Oleate of mercury..... 1 Gm.
 Glycyrrhiza, in fine powder 10 Gm.
 Athæa, in fine powder... 15 Gm.
 Glycerin..... 9 Gm.
 Honey of rose..... 32 Gm.
 M. Sig.—Blue Pill.

Triturate oleate of mercury and the mercury with the honey of rose and glycerin until it is extinguished. Then gradually add the glycyrrhiza and althæa, and continue the trituration until globules of mercury are no longer visible under a lens magnifying at least ten diameters.

Make twenty grams.

13

- R. Massæ hydrargyri..... q. s.
 Fiat pilulæ viginti, ana..... 0.325
 Sig.—“Blue Pills.”
 Nocte una sumenda.

Roll, cut and finish these on the pill machine without using the finisher or fingers to round them.

Do not weigh the mass, but return what is left to the container. Weigh the finished pills.

14

- R. Aloes..... gr. ij
 Massæ hydrarg. gr. j
 Resinæ podophylli..... gr. ½
 M. Ft. pil. tales xij no.
 Sig.—Cathartic pills.

This will mass more easily in a warm mortar. Add a little soap and water if needed.

15

- R. Hydrarg. chlorid mitis..... 1.5
 Cambogiæ..... 0.4
 Resinæ Jalapæ..... 0.5
 Ext. colocynth comp..... 2.0
 Fiant pilulæ xxv no.
 Sig.—Compound Cathartic Pills.

Mass with syrup.

16

- R. Phosphori..... 0.065
 Glycyrrhizæ pulv..... 4.000
 Tragacanthæ pulv..... 0.300
 M. Ft. pil. lx no.
 Sig.—“Phosphorus pills.”

To weigh the phosphorus, counterpoise a small capsule or watch-glass containing a little water, cut off a piece of phosphorus under water of the judged size, dry by pressing between filter-paper, drop into the water and weigh.

If too heavy take out, *again counterpoise the water*, and repeat until the desired weight is obtained.

Dry the weighed phosphorus as before, and put into a test-tube with 6 cc. of chloroform. When dissolved, pour upon the licorice powder in the mortar, stir gently to distribute the liquid through the mixture and favor evaporation.

When the chloroform has mostly evaporated and the powder is still decidedly moist, add the tragacanth and ten drops of glycerin. Work together and add enough syrup to make a mass.

Coat the pills as soon as finished with tolu.

- 17
- R. Phosphori..... 0.06
 Althææ pulv..... 6.00
 Acaciæ pulv..... 3.00
 Glycerini..... 0.63
 Syrupi..... q. s
 Chloroformi..... 6.00
 M. Fac pilulas xx no.
 Sig.—Phosphorus pills.
 Weigh the phosphorus carefully (see preceding R.), dry with filter-paper and dissolve in the chloroform. Pour this solution upon the powdered althæa, stir to diffuse it thoroughly, and when the chloroform has almost (not entirely) evaporated add the acacia and glycerin, and enough syrup to make a mass. Mass quickly. Coat the pills with tolu.
- 18
- R. Sodii bicarbonatis..... 1.30
 Pulv. rhei..... 0.650
 Olei menthæ viridis..... 0.325
 M. Ft. pil. x no.
 Sig.—“Soda-mint pills.”
 Mass with glucose excipient or with glycerin.
- 19
- R. Ferri reducti..... 0.130
 Fiat pil. no. i.
 Mitte L.
 Sig.—“Reduced iron.”
 Triturate the iron with one-tenth its weight of powdered extract of licorice and mass with glucose excipient.
- 20
- R. Aloini..... gr. $\frac{1}{8}$
 Strychninæ sul..... gr. $\frac{1}{8}$
 Ext. belladonnæ..... gr. $\frac{1}{8}$
 M. Ft. pil. tales xxx no.
 Sig.—A. S. & B. pills.
 Mix the strychnine with the aloin, then with 20 grains of powdered licorice root. Soften the ext. belladonna with syrup, incorporated with the mixed powders and mass with syrup.
- 21
- R. Strychninæ sulphat..... 0.065
 Acid arsenosi..... 0.065
 Ferri sulphat exsiccati..... 0.650
 M. Ft. massa in pil. x dividenda.
 Sig.—Iron, arsenic and strychnine.
 Mix well, according to art, and use 0.5 Gm. powdered extract of licorice, and glucose as excipient.
- 22
- R. Quininæ sulphatis..... 3 ss
 Ferri reducti..... 3 j
 Acidi arsenosi..... gr. ij
 Spiritus glonoini..... 3 ss
 M. Ft. massæ et in pil. xxx no. divide.
 Nitroglycerin explodes if triturated dry. Mix well the first three ingredients, add the spirit, and stir quickly and lightly, in order to diffuse it, add the excipient (glucose, mucil. tragac., etc.) and mass before the spirit can evaporate.
 (Do not allow to come in contact with the skin.)
- 23
- R. Opii pulv..... gr. vj
 Plumbi acetat..... gr. xij
 M. Ft. pil. xij no.
 Sig.—Lead and opium.
 (State excipient used.)
- 24
- R. Plumbi acetatis..... gr. xvj
 Camphoræ..... gr. xij
 Opii pulveris..... gr. ij
 Bismuthi subnit..... gr. xij
 Ext. gentianæ..... q. s.
 Misce fiat massa et in pil. duodecim divide.
 Sig.—“Thompson's Diarrhoea Pills.”
- 25
- R. Calcis sulphuratæ..... gr. j
 Sacchari lactis..... gr. viij
 Misce fiat pilulæ viij no.
 Conspergentur cinnamomo.
 Sig.—“Calcium Sulphide.”
 Use mucilage of tragacanth as excipient.

26

- R. Camphoræ,
Tinct. valerianæ.....aa gr. vj
M. Ft. pil. xij no.
Conserga pulvero aromatico.

27

- R. Potassii permanganatis..... 1.30
Fiat pil. no. x.
Sig.—Permanganate pills.

Powder the permanganate and mix with 1 Gm. of kaolin or of talcum. Mass with petrolatum, to which a little paraffin has been added. (Melt together 0.2 Gm. paraffin and 0.6 of petrolatum for excipient.) Use horn spatula and cut on pill-tile; avoid contact with metals.

28

- R. Potassii permanganatis,
Ferri reducti.....aa 5 j
Quininæ sulphatis..... 5 iss
M. Fiat pilulæ xlvij no.

Mix the permanganate with half a drachm each of petrolatum and paraffin, previously melted together, add the iron, then the quinine. If too soft stiffen with a little kaolin or talcum. Use horn spatula and cut on pill-tile.

29

- R. Potass. permanganat.,
Ext. ergotæ.....aa gr. xij
M. Ft. pil. xij no.

If mixed directly, the permanganate will be decomposed, and the mass will crumble.

Make two masses, one of the extract of ergot with powdered althæa, which is then rolled into a pipe in the usual manner, cut into 12 parts and each part flattened into a disc; mass the permanganate with petrolatum, roll into pills, powder well with talcum and place the pills so made in the center of the ergot discs. Now fold the discs around the permanganate pills, roll into shape and coat with tolu. This gives a permanganate pill at the center, a coating of extract of ergot, and a final protecting coating of tolu. (H. Wyatt, Jr.)

30

- R. Pilulæ argenti nitratis..... gr. ss
No. vj.
Sig.—One in the morning, fasting.

Make in the same way as permanganate pills. Or mix with 3 grains of Venice turpentine, then add sufficient powdered charcoal to make a mass and divide. These can be gelatin coated.

31

- R. Ferrous sulphate, granulated..... 16 Gm.
Potassium carbonate.... 8 Gm.
Sugar..... 4 Gm.
Tragacanth, in fine powder 1 Gm.
Althea, in fine powder... 1 Gm.
Glycerin.....
Water, each a sufficient quantity to make 100 pills.....
Sig.—Blaud's pills.

"Rub the carbonate of potassium, in a mortar, with a sufficient quantity (about 5 drops each) of glycerin and water, then add the ferrous sulphate and sugar, previously triturated together to a uniform powder, and beat the mass thoroughly, until it assumes a greenish color. When the reaction is complete, incorporate the tragacanth and althæa, and, if necessary, add a little more water, so as to obtain a mass of a pilular consistence. Divide this into one hundred (100) pills."

"These pills should be freshly prepared when wanted."

32

- R. Reduced iron..... 4 Gm.
 Iodine..... 5 Gm.
 Glycyrrhiza, in fine powder 4 Gm.
 Sugar, in fine powder..... 4 Gm.
 Extract of glycyrrhiza, in
 fine powder..... 1 Gm.
 Acacia, in fine powder..... 1 Gm.
 Water.....
 Balsam of tolu.....
 Ether, each a sufficient
 quantity to make one
 hundred pills.....
 M. Sig.—Blanchard's pills.

To the reduced iron, contained in a small mortar, add 6 cc. of water, and then, gradually, the iodine, constantly triturating until the mixture ceases to have a reddish tint. Then add the remaining powders, and mix the whole thoroughly. Transfer the mass to a porcelain dish, and evaporate the excess of moisture on a water-bath, with constant stirring, until the mass has acquired a pilular consistence. Then divide into one hundred (100) pills. Coat with tolu.

Make 50 pills. Avoid evaporating too much. The mass stiffens considerably on cooling.

33

- R. Strych. sulph..... gr. iss
 Aloini..... gr. iij
 Iodi..... gr. j
 Ferri reducti..... 3 j
 Ext. quassia..... gr. xlv
 M. Fiant pilulæ no. xxx.

Place ten grains of the iron in a mortar moistened with ten minims of a mixture of water and glycerin and add the iodine. Stir until the color of iodine has disappeared (showing complete formation of ferrous iodide), add the remainder of the iron, then the strychnine and aloin and incorporate the extract. Roll into pills.

34

- R. Ferri valerianat.,
 Quininæ valerianat.,
 Ammonii valerianat..... āā ʒj
 M. Ft. pil. xx no. Sig.—One t. i. d.

When mixed these form a semi-fluid mass. Althea should be added to stiffen and no other excipient is needed.

35

- R. Iodoformi,
 Creosoti,
 Benzoini,
 Toln..... āā gr. j
 M. Ft. pil. tales xij.

36

- R. Lupulini,
 Camphoræ..... āā gr. x
 M. Ft. massa in pilulæ decem
 dividenda.

Powder the camphor by means of a little ether, mix with the lupulin, work thoroughly and roll. The massing is hastened by using a warm mortar. No excipient is needed.

37

- R. Copaiba..... 94 Gm.
 Magnesia..... 6 Gm.
 Water at a sufficient quantity.
 M. s. a. Sig.—Copaiba mass.

"Triturate the magnesia with a little water, in a capsule, until the powder is uniformly dampened throughout. Then gradually incorporate with it the copaiba so that a uniform mixture may result, place the capsule on a water-bath, and heat during half an hour, frequently stirring. Lastly, transfer the mixture to a suitable vessel, and set this aside until the mass has acquired a pilular consistence."

Make one-fifth the quantity.

If this does not form a sufficiently stiff mass, the addition of a little resin of copaiba will usually aid in giving a proper consistency.

38

- R. Copai bæ..... 10
M. Ft. pil. no. xxx

Triturate the copaiba with 3.4 Gm. of powdered acacia, add 7 cc. of water and emulsify. Add 1 Gm. magnesia and let stand over night, then add powdered borax, incorporate and roll. (The mixture of magnesia and emulsion of copaiba may be kept in stock if desired.)

39

- R. Creosoti..... 1.0
Pulv. glycyrrhizæ rad..... 1.9
Pulv. glycyrrhizæ ext..... 1.0
Glycerini..... 0.1
M. Fac pilulas no. xv. Sig.—“One-grain creosote pills.”

40

- R. Creosoti..... 3ss
Cera flavæ..... gr. x
Pulv. glycyrrhizæ..... q. s.
M. Ft. pil. xx no.
Sig.—“1 1/2 gr. creosote pills.”

41

- R. Creosoti..... 1.0
Farinæ tritici,
Syrupi..... aa q. s.
M. Ft. pil. no. xv. Sig.—“One-grain creosote pills.”

Make a stiff mass with the creosote and a sufficient quantity of wheat flour, and add a few drops of syrup or honey to impart plasticity.

42

- R. Creosoti..... gr. xxx
Saponis pulv..... q. s.
Ft. massa in pil. xx. divide.
Sig.—“1 1/2 gr. creosote pills.”

43

- R. Creosoti..... gr. xxx
Gelatini comp..... gr. xv
Ext. glycyrrhizæ..... q. s.
M. Ft. pil. x no.
Sig.—3 gr. creosote pills.

Make the gelatin compound by dissolving 11 parts of gelatin and 5 parts of sugar in 24 parts of hot water. Add the creosote before it sets.

44

- R. Olei tigllii..... m. vj
Fiat. pil. iv. no.
Sig.—Croton oil pills.

Add ten grains of flour and two grains of soap, then glucose q. s. (See No. 41.)

45

- R. Olei tigllii..... m. v.
Saponis,
Puly. acaciæ..... aa ʒ j
M. Ft. massa in pilulæ viginti numero dividenda.
Sig.—Croton oil, 1/4 gr.

Caution must be exercised in handling this mass to avoid its irritant action on the skin.

46

- R. Lupulini..... gr. vj
Camphoræ..... gr. iss
Terebinth. Venet..... gr. xij
M. Ft. massa et in pilulas xii numero divide.

Needs licorice powder or magnesia to make a mass.

47

- R. Terebinthinæ Venetæ..... ʒ ss
Extracti hyoscyami..... ʒ ss
Pulveris rhei..... ʒ ss
Camphoræ..... gr. x
M. et in pil. xxiv divide.

48

- R. Terebeni,
Picis liquidæ..... aa ʒ ss
Balsami peruviani,
Sodii benzoatis..... aa ʒ j
M. Ft. pil. xxxv.
Sig.—One every 4 hours

- 49
 R. Chloralis,
 Camphoræ.....āā gr. xviii
 M. Ft. pil. xij no.
 Mix the chloral and camphor thoroughly and mass with 50 grains of flour and 6 drops of syrup (or q. s.). Or, add half a drachm of melted wax, and incorporate enough powdered licorice root to make a mass.
- 50
 R. Ext. aloes..... gr. ss
 Res. podophylli..... gr. 1/4
 Cascari..... gr. 1/4
 Ol. carui..... ℥ i
 M. dent. tal. dos. pil. no. xxiv.
 Mass with mucilage of tragacanth or mucilage of acacia. (Lascoff.)
- 51
 R. Acidi salicylici..... gr. lx
 Sodii acid-oleati..... gr. lx
 Phenolphthalein..... gr. xxxvi
 Mentholis..... gr. viii
 M. Ft. massa et in pil. no. xxxvi divide.
 Sig.—One every 3 hours.
 These liquefy when mixed and must be massed with an absorbent powder. Flour, or licorice with extract of licorice, makes a suitable mass.
- 52
 R. Sodii bicarb.,
 Hydrarg chlor. mitis.....āā gr. x
 Ext. cascara sagrad..... 3 ss
 Aloini..... gr. iv
 M. Ft. pil. no. xx.
 The extract of cascara is usually acid in reaction and slowly reacts with the bicarbonate, liberating carbon dioxide and causing the pills to swell. Powdered extract of cascara should be used. (Cook.)
- 53
 R. Spir. glycerylis nitrat.... 6.5 Gm.
 Althæa..... 6.5 Gm.
 Confect. rosæ..... q. s.
 M. Ft. pil c. no.
 Sig.—Nitroglycerin pills, 1/100 gr.
 To the althæa add the spirit of nitroglycerin and allow to stand until dry, *carefully avoiding* heat. Then mass and divide. (Wear rubber gloves.)
- 54
 R. Hydrarg chlorid mit
 Sodii bicarbonatis.....āā gr. x
 Ext. cascara sagrad..... gr. xxx
 Aloini..... gr. iv
 M. Ft. pil no. xx.
 The extract of cascara must be made slightly alkaline before adding the bicarbonate or the acids in the extract will slowly liberate carbon dioxide and make a troublesome and very bulky mass.
- 55
 R. Oleoresinæ capsici..... gr. xx
 Pancreatini..... gr. xv
 Pulv. zingiberis..... 3 ii
 Carbo ligni..... 3 ii
 M. Ft. pil xv no.
 The size of the pills can be reduced somewhat by evaporating two drachms of fluidextract of ginger to an extract and using in place of the powder. The pills should be coated (preferably with silver).

Prescriptions from State Board Examinations

FOR CRITICISM AND PRACTICE

- | I | 2 |
|-------------------------------|---------------------------------|
| R. Podophyllini..... gr. iiss | R. Massæ hydrarg..... gr. xv |
| Pulv. ipecac..... gr. iii | Ferri et quinin cit..... 3 ss |
| Ext. physostig., | Ext. colocynthid. co..... gr. x |
| Ext. belladonnæ, | M. Ft. pil no. v. |
| Ext. nucis vom.....āā gr. ii | Sig.—One t. i. d. p. c. (Ill.) |
| Misce bene et fiant pilule | |
| no. xii. | |
| Sig.—One at bedtime. (Tex.) | |

3

R. Phenylis salicylatis..... 3 ss
Fiat pilulæ no. vi.
Sig.—One every 4 hours. (Mass.)

5

R. Pil. atropinæ sulph.... gr. 1/20
Mitte xii. (Ind.)

7

R. Aloes..... gr. viii
Ferri reducti..... gr. xii
M. et ft. pil. no. viii. (Mass.)

9

R. Acidi arsenosi..... gr. 1/2
Strychninæ sulph..... gr. 1/3
Morphinæ sulph..... gr. ii
Ext. aconiti..... gr. ii
Quininæ sulph..... gr. x
M. et fiat pil. no. xx.
Sig.—One pill 4 times daily. (Vt.)

11

R. Acidi arsenosi..... gr. iss
Mass. ferri carb..... 3 iiss
M. Ft. pil. xxx no.
Sig.—One after meals. (Wash.)

13

R. Ferri sulph. exsic.,
Ext. bellad.,
Ext. nuc. vom..... āā gr. ss
Pil. rhei co..... gr. ii
M. Ft. pil. no. x.
Sig.—Una nocte manequē sumend.
(Br. Col.)

15

R. Hydrarg. chlor. corros..... 0.065
Ammonii chlor..... 2.000
M. Ft. pil. no. xii.
Sig.—One as directed. (Ill.)

17

R. Strychninæ sulph..... gr. 1/30
Acidi arsenosi..... gr. 1/60
Ferri reducti..... gr. i
Ext. gentianæ..... q. s.
M. Ft. pil. d. t. d. no. xxx.
Sig.—Unam t. i. d. (N. Y.)

4

R. Quininæ sulphat..... gr. xx
In pil. no. x. divide
Sig.—One every 4 hours. (Ill.)

6

R. Aloini..... 0.15
Ext. belladonnæ..... 0.06
Ext. nucis vom..... 0.04
M. Ft. pil. no. iv. (Wash.)

8

R. Quininæ sulph..... 3 i
Arseni trioxidi..... gr. x
Ferri sulph. exsic..... gr. xxx
Aloini..... gr. i
M. Ft. pil. no. xxx.
Sig.—Take one 3 times a day.
(Tex.)

10

R. Iodi..... gr. i
Ferri iodidi..... gr. x
Potass. iodidi..... gr. xx
Ext. conii..... gr. x
Misce ft. massa et in pil. x div.
Sig.—One 3 times a day. (Wash.)

12

R. Camphoræ monobrom..... gr. xii
Ext. belladonnæ..... gr. ii
Pulv. saponis..... q. s.
Misce et in pil. no. xii divide.
Sig.—One at bedtime. (Wash.)

14

R. Phenylis salicylat..... gr. xv
Camph. monobrom..... gr. x
Acetanilidi..... gr. xv
M. Ft. pil. no. x.
Sig.—One at night. (Ill.)

16

R. Camphoræ monobrom..... gr. xi
Ext. belladonnæ..... gr. ii
Pulv. saponis..... q. s.
M. Ft. pil. no. xii.
Sig.—One at bedtime. (S. D.)

18

R. Bismuthi subnit..... 3 ss
Sodii bicarb..... gr. xv
M. Ft. pil. no. x.
Sig.—One pill after meals as
directed. (Ill.)

19

- R. Ferri sulph. exsic. gr. i
 Quin. sulph. gr. ss
 Strych. sulph. gr. 1/20
 Res. podophyl. gr. 1/4
 Pil. rhei co. gr. ii
 M. Ft. pil. Mitte x.
 Sig.—Pil. una b. i. d. per hebdom
 sumend. (Br. Colum.)

21

- R. Pulv. opii. gr. v
 Bismuthi subnit. 3 i
 Sodii bicarb. gr. xx
 M. Ft. pil. no. xx.
 Sig.—One every 2 hours. (N. C.)

23

- R. Acidi arsenosi. 0.001
 Ferri sulphatis. 0.100
 Potassii carbonatis. 0.100
 Pulv. tragacanthæ. q. s.
 M. Ft. pil. d. t. d. no. xx. (N. Y.)

25

- R. Potass. permang. gr. x
 Ft. mass et div. in pil. no. x.
 Sig.—One every 4 hours. (Mo.)

27

- R. Aloini. gr. iv
 Strychninæ. gr. 1/60
 Ext. bellad. gr. 1/8
 Ipecac. gr. 1/16
 M. Ft. pil. tales no. c. (Ga.)

29

- R. Strychninæ sulph. 0.001
 Arseni trioxid. 0.003
 Quininæ sulph. 0.12
 Massæ ferri carb. 0.24
 Mitte pilulas tales no. lx.
 Sig.—One pill 3 times a day. (N. J.)

31

- R. Ext. nucis vomicæ. 0.01
 Potassii carbonatis. 0.15
 Ferri sulphatis gran. 0.15
 Extracti glycyrrhizæ. q. s
 M. Ft. pilulæ parvæ d. t. d. numero
 duodeviginti.
 Sig.—Capiat unam omni quarta hora.
 (N. Y.)

20

- R. P. rad. rhei. ʒ i
 Aloes. socot. gr. xv
 P. myrrhæ,
 Sapo dur. āā ʒ ss
 Ol. menth. pip. gr. ii
 Syr. glucosi q. s. ut fiant. pil. xx
 quarum ij deglut hor. decub.; dilu-
 culo pulv. sod. tart. eff. sum.
 (Br. Col.)

22

- R. Ext. colocynthi comp. 0.60
 Ext. hyoscyami. 0.30
 Resinæ jalapæ. 0.20
 Ext. leptandræ. 0.15
 Resinæ podophylli. 0.15
 M. et in pil. x divide.
 Sig.—As directed. (N. Y.)

24

- R. Aloini. 0.130
 Strychninæ. 0.006
 Ext. bellad. 0.080
 Ipecacuanhæ. 0.040
 Glycyrrhizæ. 0.460
 Syrupi. q. s.
 M. Ft. pilulæ no. x.
 Sig.—One or two pills at bedtime.
 (Col.)

26

- R. Quininæ muriat. 2.000
 Acidi arsenosi. 0.016
 Ferri reducti. 1.000
 Ext. gentianæ. q. s.
 Misce fac pilulas no. xv.
 Sig.—One b. i. d. (Vt. and Tex.)

28

- R. Strychninæ sulph. gr. iii
 Quininæ sulph. gr. xx
 M. Ft. pil. no. xv.
 Sig.—One t. i. d. (Okla.)

30

- R. Ext. nucis vom. 0.015
 Aloini. 0.030
 Hydrarg. chlor. mit. 0.060
 Ext. hyoscyami. 0.045
 M. Ft. pil. no. i. Mitte xxiv.
 Sig.—One at night. (La.)

32

- R. Fellis bovis purif. 0.6
 Saponis medicati. 0.5
 Pulv. rhei. 0.7
 Ext. taraxaci quantum sufficit.
 M. Ft. pil lege artis. Divide æqualis
 duodeviginti.
 Conspurgantur cassia cinnamoma
 pulvurata. (N. Y.)

33

- R. Potassii permanganatis..... gr. ii
 Extracti belladonnæ..... gr. v
 Extracti taraxaci..... q. s.
 M. et fiat pilulæ xx no.
 Sig.—One pill twice a day.

35

- R. Ext. digitalis..... 0.2
 Pulv. scillæ..... 1.0
 Pulv. nucis vomic..... 0.5
 Misce, ft. massa et divide in partes
 æquales, pilulæ decem (parvæ).
 Sig.—Capiat unam. p. r. n. (N. Y.)

37

- R. Hydrarg. chlor. mit. gr. pars quarta
 Pulv. aloes..... gr. unum
 Pulv. rad. rhei.... gr. semissem
 Syrupi q. s. ut ft. pilula dentur
 tales doses duodecim consperge
 cum pulvere cassiæ
 Sig.—Two pills at night. (Mo.)

39

- R. Ferri sulph exsic..... gr. xxv
 Quininæ sulph..... gr. xxv
 Arseni trioxid..... gr. i
 M. Ft. pil xxiv no.

34

- R. Creosoti puri..... 0.4
 Pulv. althææ..... 0.3
 Pulv. gentianæ..... 0.4
 Glycerini..... 0.2
 Extracti et pulveris
 Glycyrrhizæ q. s.
 Misce, fiat pilulæ numero quindecim.
 Sig.—Capiat unam omni quarta
 hora. (N. Y.)

36

- R. Quininæ sulph..... gr. i
 Morph. sulph..... 3 i
 M. Ft. pil. xii. no. (Tex.)

38

- R. Camphoræ..... 1.2 Gm.
 Mentholi..... 0.6 Gm.
 Ext. glycyrrhizæ..... q. s.
 M. et fit. pil. parv. no duodevigniti.
 Sig.—Capiat unam omni tertia hora.

40

- R. Ferri sulph..... 1.6
 Potass. carb..... 0.8
 Sacchari..... 0.4
 Tragacanthæ..... 0.1
 Althææ..... 0.1
 Glycerini
 Aquæ..... āā q.s.
 M. Ft. pil no. x.
 Sig.—Pil ter vel quat in die. (Col.)

CHAPTER IX

LOZENGES, PASTILS, ETC.

Lozenges are small discs of medicated or flavored sugar, intended to be dissolved in the mouth. The word *lozenge* is used in a broad sense, and refers to the form in which the medicinal matter is stored or administered. It may be applied to troches, tablets, pastilles, etc., all of which are broadly called lozenges, but the other terms are used in a more restricted sense.

Troche (Lat. *Trochiscus*, *i*) (pronounced trôch or trô'kē), a lozenge composed of medicinal ingredients mixed into a paste with sugar and mucilage and dried. It is intended to be gradually dissolved in the mouth and slowly swallowed, producing a demulcent effect.

Pastil or Pastille (pas-tel') (Lat. *Pastillus*, *i*).—The Latin word *pastillus* is the diminutive for *panis*, a loaf, and thus means properly a little loaf. In pharmacy the word is

used somewhat indefinitely, referring mostly to lozenges having gelatin and glycerin, or chocolate for a base.

Chocolate lozenges are called pastils in the German Pharmacopœia, but "*tabellæ*" in the British.

Fumigating pastils are little cone-shaped compounds of balsam, spices, etc., with charcoal or other combustible substances as a base, designed for burning as a fumigator or disinfectant.

Bacill (Lat. *Bacillula*, *æ*), a short, rod-like lozenge corresponding to troche, except in shape. It is a more convenient form for the small troches.

Lamel (Lat. *Lamella*, *æ*).—Minute glyco-gelatin discs medicated for use in the eyes or for hypodermic injections.

Orbicules or Globules (Lat. *Rotula*, *æ*), are hemispherical globules of sugar, medicated by dropping upon their surface a volatile oil, which is absorbed.

These classes of preparations, though largely sold in drug stores, are not made to any considerable extent by pharmacists.

They are, properly, medicated candies, and require special apparatus and skill to obtain tempting products. The numerous candy cough-drops are included here, which might be included in the domain of pharmacy but that they require a skill in the manipulation of melted sugars and special moulds, work-benches, etc., which will confine them to the work of the manufacturing confectioners.

Many of the smallest medicated lozenges are coated heavily with sugar, and are thus rendered more candy-like, while the chocolate lozenges and the bacillula suggest other familiar forms of confectionery.

In the following pages only such forms of lozenges are treated as are official in the principal pharmacopœias, and are liable to be prescribed by physicians, or can be profitably made in the pharmaceutical laboratory.

Troches are made of various forms, the more common being round or rectangular. The manufacturers, by whom most of the troches at the present time are made, use dies of various shapes and sometimes arranged to stamp some name or design upon the face of the troche.

Such dies consist of a metallic cylinder with a cutting edge, into which is sometimes fitted a plunger, bearing upon its face the design

in bas-relief or intaglio, which, being forced upon the soft mass, leaves its impression upon the troche. The mass, having been rolled into a flat sheet, either upon a troche board or between adjustable metallic rollers, is then cut by hand with these dies, the latter being either single or in sets.

A **troche-mass** consists of medicinal matter, mixed with sugar and gum, made into a dough by means of syrup or honey. When no dry gum is used the mass is made with mucilage. It should be made softer than a pill mass, so that it may be moulded and flattened without cracking. Moistening agents should be added very cautiously, since sugar softens by kneading, and a little liquid which appears to be insufficient to produce plasticity, may, upon being well worked in, produce a mass which lacks firmness. When the troche contains acacia, it is usually mixed with the sugar in dry form, but when tragacanth is used the mucilage of tragacanth is preferred as an excipient.

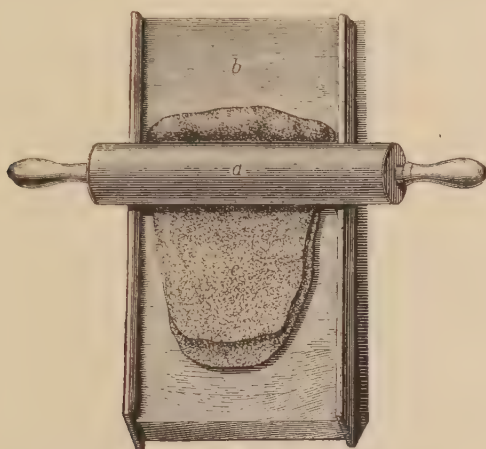


FIG. 25.—Lozenge board and roller.

The choice of these two gums depends upon the purpose of the troche as well as upon its ingredients. Acacia makes a more tenacious troche which dissolves more slowly than when tragacanth is used.

It is to be preferred, therefore, for throat lozenges and such as are desired to dissolve slowly. The proportion of gum present controls to a large extent the rate of solubility.

The sugar should be in a very fine powder, or the surface of the troche will not be smooth. That sold under the name of "confectioners' sugar" is best to use. It has been recommended to reserve a portion of the sugar from the mass until the excipient has all been added and kneaded in, then the reserve portion is incorporated; this is to avoid an unduly soft mass, but such proceeding is not necessary if the excipient be added cautiously.

White of egg and syrup of marshmallow are sometimes used as excipients in place of mucilage. These do not make as hard a troche, unless gum is also present, but they are very palatable. For laxative troches prune-paste is an agreeable excipient.

If a troche-board and cutter is at hand, the mass is now weighed, and the weight divided by the number of troches desired. The weight of one troche having thus been ascertained, the amount is weighed out and formed into a troche in the cutter, in order to ascertain its thickness. The sides of the troche-board are now adjusted to correspond to this, and the entire mass rolled into a sheet of corresponding thickness, which is then cut into troches by means of the cutter.

Rotary cutters are used by candy manufacturers which are very convenient for pharmacists when a number of lozenges are to be cut. It consists of a wheel on the rim of which are the cutting edges.

In rolling and cutting the mass a dusting-powder is usually necessary. Powdered sugar of milk is usually best for this, being less hygroscopic than cane sugar, and less quickly absorbed by the mass. Starch is also used. When dark-colored troches are made, an aromatic powder, as cinnamon, orris, etc., may be employed in very sparing

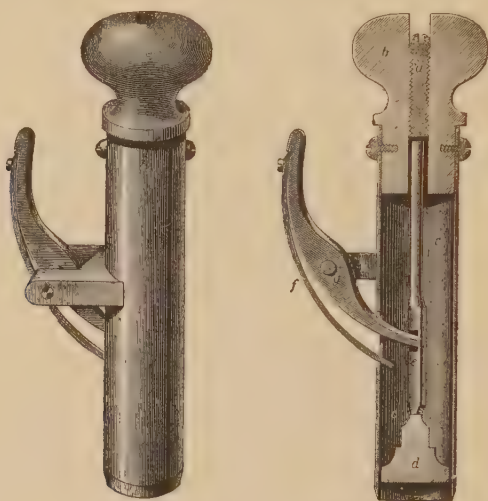


FIG. 26.—Lozenge cutter.

quantities. These should be avoided, unless the aromatic flavor will harmonize with that of the troche. Less powder will be needed if the mass is rolled and cut upon paraffin paper. Few stores are provided with troche apparatus, because most of these medicaments are now made by the large manufacturers. A fairly good troche can be made, however, without the use of special apparatus, and no pharmacist need turn away a prescription for a troche which he does not keep in stock because of the lack of such convenience. If a troche-cutter is at hand the mass may be rolled into a sheet upon the pill-machine or tile by means of a round, smooth-sided bottle. Or in the absence of a troche-cutter the mass is first made into boli, in the same manner as making pills. These, after having been well rounded, are pressed into a flat form by means of a broad spatula or a flat board, care being taken to have all of the same size. A good method is to flatten a number together upon the pill-machine, using the raised sides of the machine as a

gauge for thickness. Very good-looking troches can be made in this way if the mass is made very soft. With a dry or stiff mass the edge of the troche will crack and be uneven, but with a soft mass a smooth and round edge is obtained. The mass should always be divided as soon as made.

Instead of flattening the bolus with a spatula or board, a troche-former may be used. This consists of a smooth metallic tube about three inches in length, the diameter of which is the same as that of the troches desired. Into this is fitted, not too tightly, a rod of wood or metal which is used as a plunger and is longer than the cylinder.

The tube is now placed in an upright position over the bolus, so that the latter rests upon the pill-til inside the tube. The plunger is then pressed gently upon the bolus and the latter is thereby formed into a troche.

If the bottom of the plunger has cut into or raised upon its surface a suitable design the latter will appear in reverse upon the surface of the troche.

Another method of forming the troche is to force the mass through a glass tube, which has been slightly greased on the inside, and cut the mass into lozenges as it emerges.

All troches should be partially dried before being delivered. In most cases drying in a warm place—as near a stove or radiator—for about an hour is sufficient; but when the troches contain volatile ingredients, essential oils, etc., heat should be avoided. These should be dried in a desiccator, which may be readily improvised by placing them in a tight pasteboard or wood box, alongside a lump of quicklime. The lime abstracts the water greedily, but does not affect the oils.

Troches which contain poisonous substances should either be colored or stamped in such a way as to warn against their too free use. Commercial santonin lozenges are usually colored pink for this reason.

BACILLS

Short, rod-like lozenges are the form in which the smallest troches are sometimes preferred. They are also dispensed in the place of round troches when special apparatus for these are wanting.

They may be made by rolling the mass into a pipe, as in making pills, then cutting into short lengths, or a smoother surface may sometimes be obtained by flattening the pipe between the cutters of the pill machine, so that it is forced into the grooves.

In the German Pharmacopœia this form is directed for troches weighing less than ten grains.

PASTILS

Pastils or pastilles (pronounced pas'-til or pas-tel') are soft lozenges, having, usually, gelatin or chocolate for a base. Glycerin is associated with the gelatin to keep the mass soft.

A formula which is popular in England is gelatin one part, glycerin and water each two and one-half parts by weight. The gelatin is softened in the water by aid of heat, and then the glycerin is added and the heat continued until a clear solution results. This sets on cooling to a firm, transparent jelly, which dissolves slowly in the mouth.

Medicinal agents are added just before the solution stiffens, and stirred until the mass becomes firm enough to remain homogeneous. When insoluble powders are added they should first be made into a stiff paste with a little glycerin.

The pastils are flavored with fruit juices and acids, with aromatics, etc.

Rose water, cinnamon-, orange flower-, or bitter almond-water may be substituted for the water used to dissolve the gelatin. Glycyrrhizin in the proportion of 24 grains to 1 ounce of gelatin makes a good flavor for pastils of ammonium chloride.

The pastils may also be colored with carmine if desired.

To form the pastils the melted mass is allowed to congeal upon a flat surface, having raised sides or edges, so that it will form a square or rectangular sheet of the size and thickness desired. When cold this

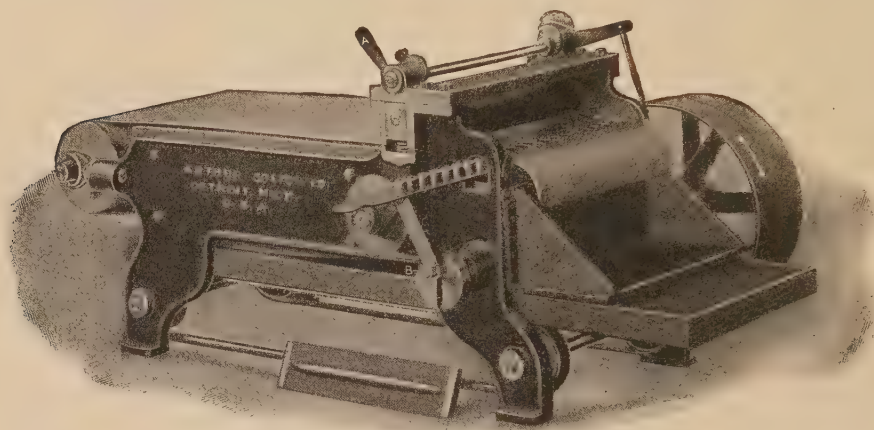


FIG. 27.—Lozenge machine.

is cut into squares with a sharp knife. Moulds can be obtained of glass or tin which have the bottom marked with lines to indicate the squares of the finished troche, and any measurements are unnecessary. In the absence of these fairly good results may be obtained by allowing the mass to congeal in the bottom of a tin seidlitz-powder box, or in the pasteboard cover of a powder box of suitable size, which has previously been oiled to prevent sticking.

The sheet of gelatin is then taken out and cut into suitable pieces by eye or measurement.

Professor Bergy recommends the use of brass bars which are employed by candy manufacturers for making forms. Those which he uses are $\frac{3}{42}$ " $\times$ $\frac{3}{4}$ " $\times$ 16 inch, and are placed on a glass plate to form a square or rectangle of any desired size within the limits of the bars. The pastille mass is poured inside, and when it has set the bars are removed and the mass is cut.

Pastils containing active ingredients of a volatile or changeable character should be freshly prepared, but in many cases these can

be kept for a considerable time if coated with gelatin while fresh. Unless otherwise specified, pastils of gelatin should weigh about thirty grains each.

A more slowly soluble mass for throat affections may be obtained by addition of acacia. A good formula is: Gelatin, 1 ounce; glycerin, 2 1/2 ounces; acacia, 2 drachms; aromatic water, 2 ounces.

A still more slowly soluble mass is made without gelatin as follows: 18 parts of gum acacia and 6 of sugar are dissolved in 80 parts of water, and the solution is strained. It is then evaporated to 30 parts, the medicinal agent added, and the mixture, after it has become transparent, is poured into moulds.

Chocolate pastils are made by fusion in a similar manner to those of gelatin, or by the cold method in a manner similar to the making of troches and bacills. The commercial sweet chocolate may be used, or a mixture of equal parts of cacao butter and sugar with one-fourth to one-half these quantities of cocoa, as best suits the case. The latter is preferable for pastils which contain much insoluble or liquid matter.

The same precautions must be taken in handling of these as in suppositories, which they closely resemble from a manufacturing standpoint. Tragacanth is sometimes recommended to make the mass more adhesive (when some water must be present) and saccharin is also used as a sweetener.

In many cases the sweet chocolate of the market, with addition of a little cacao butter and sugar, suffices for a good mass.

Paraffin may be added if too soft.

LAMELS

Lamels are minute discs of glycerinated gelatin, containing small doses of active medicinal matter. They are used chiefly in ophthalmic treatment in place of collyria, or for producing dilation or contraction of the pupil, producing anæsthesia, etc. They are made very thin and small, so that they can be inserted underneath the lids.

They may also be used for extemporaneous preparation of hypodermic solutions.

In the British Pharmacopœia three were official, one containing $\frac{1}{5000}$ grain of atropine sulphate, one of $\frac{1}{200}$ grain of cocaine hydrochloride and one containing $\frac{1}{1000}$ grain of physostigmine in each lamel.

SUGAR GLOBULES OR ORBICULES

These are small hemispherical globules of sugar made by heating sugar with water until a stiff, pasty mass is obtained, then dropping upon a cold polished surface in such a way as to obtain little half-rounded lozenges of sugar similar to the peppermint drops of the market. These are medicated as desired, with volatile oils, dropped upon the globules. When very small quantities of oils are administered in this way, the oil is first diluted with alcohol or ether and the globules saturated with this mixture.

The globules thus correspond to the sugar-pellets of homœopathic pharmacy, except in size and shape, and like them are always obtained from confectioners ready for medication. They are official in the German Pharmacopœia under the title *Rotulæ Sacchari*.

TROCHES

1

- R. Tincture of ginger..... 20 cc.
 Tragacanth, in fine powder..... 4 Gm.
 Sugar, in fine powder .. 130 Gm.
 Syrup of ginger, a sufficient quantity to make 100 troches.
 M. Sig.—Troches of ginger.

"Mix the tincture of ginger with the sugar, and, having exposed the mixture to the air until dry, reduce it to a fine powder. To this add the tragacanth, and mix thoroughly. Lastly, with syrup of ginger, form a mass, to be divided into one hundred (100) troches."
 Make 20 troches.

2

- R. Potassium chlorate, in fine powder..... 30 Gm.
 Sugar, in fine powder .. 120 Gm.
 Tragacanth, in fine powder..... 6 Gm.
 Spirit of lemon..... 1 cc.
 Water, a sufficient quantity. Make 100 troches.
 Sig.—Potassium chlorate troches.

"Mix the sugar with the tragacanth and the spirit of lemon by trituration, in a mortar; then transfer the mixture to a sheet of paper, and, by means of a bone spatula, mix with it the potassium chlorate, being careful, by avoiding trituration or pressure, to prevent the mixture from igniting or exploding. Lastly, with water, form a mass, to be divided into one hundred (100) troches."
 Make 20 troches.

The powders must be mixed and massed very cautiously, as the dry mixture is explosive by friction or pressure.

3

- R. Prepared chalk..... 25 Gm.
 Acacia, in fine powder..... 7 Gm.
 Spirit of nutmeg..... 3 cc.
 Sugar, in fine powder .. 40 Gm.
 Water, a sufficient quantity. Make 100 troches.
 Sig.—Troches of chalk.

"Rub the powders with the spirit of nutmeg until they are thoroughly mixed; then, with water, form a mass, to be divided into one hundred (100) troches."

Make 20 troches.

4

- R. Charcoal..... 30.0
 Tragacanth, powdered..... 4.0
 Sugar, powdered..... 66.0
 Vanillin..... 0.3
 Water a sufficient quantity to make 100 troches.
 Sig.—Charcoal lozenges.

5

- R. Quinine tannate..... 6.0
 Tragacanth, powdered..... 3.0
 Cacao butter..... 5.0
 Prepared cocoa..... 25.0
 Sugar, powdered..... 60.0
 Vanillin..... 0.3
 Saccharin..... 0.2
 Water a sufficient quantity to make 100 troches.

Sig.—Beringer's quinine tannate troches.

6

- R. Sulphur..... 30.0
 Cream of tartar..... 6.0
 Tragacanth, powdered..... 4.0
 Sugar, powdered..... 60.0
 Oil of orange..... 0.5
 Water a sufficient quantity to make 100 troches.

Sig.—Sulphur and cream of tartar lozenges.

7

- R. Olei gaultheriæ..... 0.20
 Pulveris sacchari..... 15.00
 Mucilaginis tragacanthæ..... q. s.
 M. Ft. trochisci viginti no.
 Sig.—Wintergreen lozenges.

8

- R. Pulv. tragacanthæ..... 5.0
 Pulv. sacchari..... 15.0
 Aquæ rosæ fort..... q. s.
 M. Ft. trochisci xx no.
 Sig.—Throat lozenges.

9

- R. Pulv. glycyrrhizæ comp..... 5 iv
 Pulpæ pruni..... q. s.
 M. Ft. trochisci xxiv no.
 Sig.—Compound licorice lozenges.

10

- R. Sodii boratis..... 10
 Sacchari..... 90
 Tragacanthæ..... 0.25
 Tinct. benzoini..... 1.0
 Aquæ..... 6.0
 M. Ft. trochisci no. c.

Mix the borax with half of the sugar, and the tragacanth with the remainder of the sugar. Triturate the tragacanth-and-sugar mixture with the water, add the tincture of benzoin, triturate well, then add the borax mixture, incorporate quickly and divide into 100 troches.

(Borax coagulates gum, and a tough, elastic mass which cannot be worked, is formed if the borax is added directly to the tragacanth. The same would apply to acacia.)

11

- R. Gelatini..... 5.0
 Aquæ bullientis..... 5.0
 Glycerini..... 0.5
 Misce at adde.
 Creosoti..... 10.0
 M. Ft. emulsionis et in pastillos c
 divide.

Make an emulsion of the hot paste and creosote by rapid trituration, continued until the gelatine stiffens, then allow to congeal and divide.

12

- R. Camphoræ... gr. viij
 Menthol..... gr. iv.
 Pastæ gelatini pro pastillos. q. s.
 M. Fac. pastillos no. xij.
 Sig.—Sedative pastilles.

13

- R. Iodoformi..... gr. xij
 Pastæ gelatini pro pastillos. q. s.
 M. Ft. pastillos no. xi.
 Sig.—Iodoform pastilles.

14

- R. Ext. kola..... 1
 Pulv. chocolate..... 10
 Pulv. milk sugar..... 1
 Syrup..... q. s.
 M. make 10 pastilles.
 Sig.—Kola pastilles.

15

- R. Santonini..... 3 ss
 Hydrarg. chlor. mitis..... gr. x
 Pulv. chocolatæ..... 3 iss
 Sacchari..... 3 v
 M. Ft. pastilli xxx no.
 Sig.—Santonin lozenges.

16

- R. Hydrarg. chlor. mitis..... 1
 Chocolatæ..... 20
 Syrupi..... q. s.
 M. Ft. pastilli xv no.
 Sig.—"Calomel pastilles."

Powder the chocolate and mix the calomel thoroughly, mass with the syrup and divide.

17

- R. Olei ricini..... 10
 Pulv. theobromat. sine oleo 10
 Sacchari..... 20
 Tinct. vanillæ..... 0.50
 M. Ft. pastilli no. x.
 Sig.—"Castor oil pastilles."

Mix the oil with the cocoa (the powdered cocoa put up for making hot drinks may be used) then with the other ingredients, and roll into pastilles.

CHAPTER X

TABLETS

Tablets have largely taken the place of pills in the administration of medicines, partly because of their quicker solubility and more prompt action, and partly because they can be manufactured more cheaply than pills.

Tablets are of two kinds, the compressed tablets and the triturate tablets. They differ materially in character as well as in their method of preparation. The first are formed of *dry material in a granular condition* by compression, while the second are formed of *moist material in very fine powder* in a mould.

COMPRESSED TABLETS

The manufacture of compressed tablets involves the art of pharmacy in the proper mixing and preparation of the materials, the practise of chemistry in the treatment and prevention of reactions which may occur under heavy pressure, of mechanics in the adjustment and control of machinery, of engineering in the arrangements for proper drying and sifting of materials, and sometimes of electricity in the control and adjustment of motors. It is therefore not a strictly pharmaceutical operation, though it rests upon a pharmaceutical basis. Tablets being a sequence to pills are composed of about the same kinds of ingredients, and the initial part of the operation,—mixing, applying an excipient for the purpose of granulation and making a crumbly mass,—is essentially the same as in making pills. But then the mass is to be dried and reactions or discolorations are likely to occur under the heat. Next the granulated material is compressed under a pressure of one to six tons, and this alone will cause some reactions that do not trouble the pill-maker. Finally there is the purely mechanical phase of the operation, exhibited in the adjustment and lubrication of dies, uniform feeding of the material and the mechanical operation of turning out a smooth, unspotted and accurately dosed tablet. Therefore tablet-making is a special study which is beyond the ordinary operations of pharmacy, requiring special equipment and skill. Yet there are a number of tablets which the pharmacist can prepare satisfactorily, and there are methods which are applicable to extemporaneous needs but are not suitable for stock tablets.

The shape of tablets is limited only by the restrictions of die-making. The most common form is disc-shaped with convex surfaces, but special shapes are frequently seen. Mercuric chloride tablets for antiseptic use are highly poisonous and are made coffin-shaped and also colored blue. Special tablets are oval, triangular, rectangular, hexagonal, ring-shaped, heart-shaped or a variety of forms. They may be plain or lettered, or may show a special design. Almost any form for which dies can be made may be found in compressed tablets.

But since special designs require not only special dies, but special care in preparing the materials so that it will feed slowly and fill all parts of the die, most tablets are made round or lozenge-shaped with slightly convex surfaces.

There are four essentials in making compressed tablets, which must receive consideration. These are:

1. *To regulate the pressure carefully.*
2. *To ensure proper cohesion of the particles that are being compressed and an equal amount of material in each tablet.*
3. *To prevent adhesion of the material to any portion of the machine.*
4. *To secure readily soluble or medicinally active tablets.*

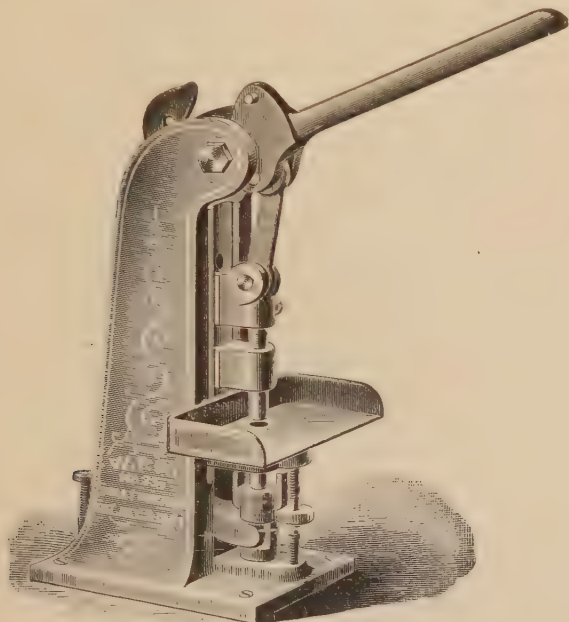


FIG. 28.—Hand tablet machine.

The first is a mechanical operation, and depends mainly upon the machine.

Tablet machines may be obtained in great variety of form and capacity, and at various costs. They vary mainly in their capacity and the variety of their uses, and in the rapidity of their action.

They may be divided into two classes—the lever machines, operated only by hand, and the geared machines, operated either by hand or by power. The first are suitable only for small operations, as the extemporaneous preparation of a very few tablets. They are fed and operated entirely by hand, and are more liable to get out of adjustment if a large number of tablets are run off upon them.

The geared machines are made for rapid and automatic action, working either by power or by hand, and are adapted for a variety of sizes and styles of tablets. These are capable of making 100 to 500

tablets per minute. A selection of a machine will depend upon the use to which it will be put, and the facilities for operating.

The most important part of the machine is the dies and their fittings. These must be of hardened steel, well fitted and perfectly smooth. Unless the dies fit well into the sockets, and are *perfectly smooth* a perfect tablet cannot be made. If there is a scratch or roughness on the surface, this will fill with the substance that is being compressed and the surface of the tablet will be broken. Every effort must be made to secure and keep smooth dies. As they become worn, burnishing or re-grinding must be done.

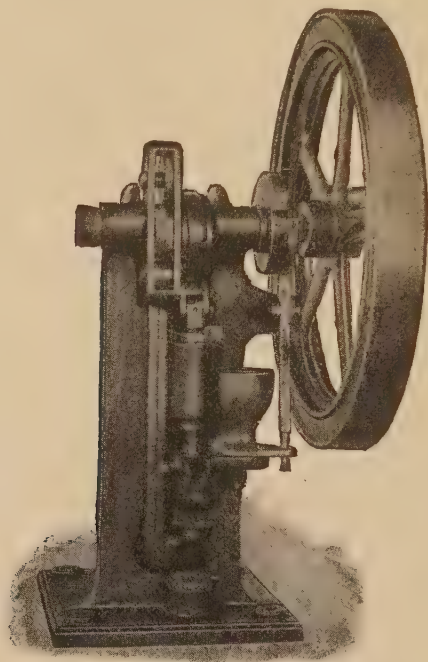


FIG. 29.—Tablet machine.

If substances adhere to the dies, they should be removed with warm water or alcohol and a soft cloth or sponge. Never dig it off with a spatula or other metallic tool. The finest machine in the world will not turn out good tablets unless the dies are in prime condition.

They must also be protected from corrosion and rust. Some substances, particularly corrosive sublimate and acid salts or acids, act upon steel, and unless the dies are protected they may be ruined by their action. If such substances are compressed, the granulated materials must be well dried, and the dies kept well lubricated. Then, immediately after finishing the tablets, the dies should be taken out of the machine, thoroughly cleaned, and well oiled.

It is advisable to keep the dies and sockets immersed in oil when not in use. The dies in the cheaper machines should be just as good as those in the more expensive machines.

The selection of a machine will depend mainly upon such questions as whether one wishes to make tablets in quantity or only as ordered; whether two size of dies are sufficient or a dozen sizes are wanted; whether the machine must be operated by hand or by power; etc. The only general suggestion that may apply, is that in selecting a machine, ease of cleaning and adjustment or change is a matter of quite as much importance as ease of operation. The working parts should be easily accessible and the dies should be easily removed or cleaned.

To operate easily, any machine requires a firm foundation. Unless the machine is to be operated by engine-power, it will be found convenient to fasten it upon a bench somewhat lower than the usual working-counter. A strong box of suitable height makes a portable stand and the interior of the box may be utilized as a container for the necessary tools.

The hardness and weight of the tablets are adjusted by the position of the compressors in the machine. The depth to which the lower die sinks in its socket determines the quantity of material which shall fill the socket, and consequently the weight of the tablet. The depth to which the upper die sinks determines the thickness and the hardness of the tablet.

The lower die is first adjusted to receive the proper quantity of material each time it is filled, and so to make tablets of a definite weight. Then the upper die is adjusted to make the tablets of the required hardness.

Except when tablets are intended to be dissolved slowly in the mouth, hard compression is not desirable. A tablet which will break easily in the fingers, and not break or chip when dropped upon the floor, is considered the proper condition for most tablets.

PREPARATION OF THE MATERIAL

While it is possible to compress fine powders into tablets, if the powders are fed slowly, the tablets will not be as smooth and even in weight as when they are made from granulated materials. Fine powders occlude air and compress unevenly, and they do not feed well into the dies.

To secure good results the material to be compressed should be in a uniformly granular condition, the granules being of such a size that they will just pass easily through a No. 40 or 60 sieve. A few special substances are made into finer granules, but these are exceptional.

Proper granulation is an essential part of tablet-making, and is often the most difficult part. The excipient used must not be markedly hygroscopic or the granules will not dry well, or remain dry. This rules out such excipients as glycerin, glucose, honey, and even syrup. The excipient must be physiologically inert, chemically compatible with the tablet ingredients, must possess some adhesive properties but not enough to materially hinder disintegration or solution.

As in pill making, absorbents may be necessary to granulate oils, resinous substances etc. and the absorbents used in pill making are generally applicable for tablets.

One condition that applies in tablet making which necessitates finer discrimination than in pill making, is the frequent necessity of

obtaining tablets which will dissolve to yield a clear solution in water. Soluble tablets are usually composed entirely of soluble chemicals which can be obtained in granular crystals and which need no further treatment, but sometimes combinations occur which necessitates granulating the mixture. Care must then be taken to select granulating agents which will not interfere with the solubility, either in readiness or clearness of solution.

Crystalline salts and chemicals are usually obtainable in small crystals which are suitable for tablet-making without any preparatory treatment. A selected size of crystal,—usually one which will pass through a number 20 or 40 sieve and will not pass through the next or second finer size—is all that is required. Larger crystals can be partially crushed and the proper size of granules separated by sifting, when this method is economical. It is only necessary to secure a size of granule which will feed uniformly in the machine and compress smoothly.

Hygroscopic and deliquescent salts are not suitable for tablets, and they are often very troublesome in combinations with other medicinals, even in small proportions. It must always be remembered that only *dry* granulated material is suitable for compressed tablets. Moist material will not feed evenly, and in most cases will not compress properly.

Vegetable drugs and non-crystalline chemicals, including extracts, resins, insoluble powders, and most mixtures containing potent remedies or more than two ingredients, need to be formed into granules by means of a suitable excipient. The first requisite is that the substance or mixture be in a fine powder. This means a powder which will pass through a number 100 sieve, or finer. The powder is then moistened with a suitable excipient, just sufficiently to cause it to cohere in small granules, when it is immediately and thoroughly dried, and, if necessary, sifted.

The excipients used are mostly starch paste or a warm gelatin solution. The starch paste is chosen for white tablets, and the gelatin solution for soluble tablets or when a greater adhesive action is needed.

In a small way the powders can be moistened by lightly working the excipient into them in a mortar, as in making a pill mass but with less pressure. Add excipient cautiously, and thoroughly work it in, to secure the granular condition. It will be found that as the powder absorbs the liquid it agglomerates into very small granules, and the object is to get these as uniform as possible. Too little excipient will leave fine powder ungranulated; too much will form masses instead of granules. If the moistening is just right the mixture may be dried and will yield the result directly.

If the moistening is slightly over done, it will be necessary to press the mixture through a sieve of proper size to form and separate the granules.

Other excipients which are used are alcohol or acetone—employed for resinous or oily materials,—mixtures of alcohol and water, or water. These excipients must have sufficient solvent action on the material to produce the adhesive qualities needed to form the granules. Syrup is rarely employed because it is difficult to dry the granules formed with it.

Drying is important, and the method is important. Rapid drying is usually a mistake, because the granules lose their moisture first from the surface and this forms a shell through which the moisture in the interior is unable to escape. Then when the granules are compressed in the machine, they break, the interior moisture is liberated and under the pressure it is increased and a discolored or soft and sticky tablet results. This gums up the dies, and the results are altogether unsatisfactory.

In manufacturing on the large scale, the drying process is begun in a moist atmosphere and relatively low temperature, and the humidity

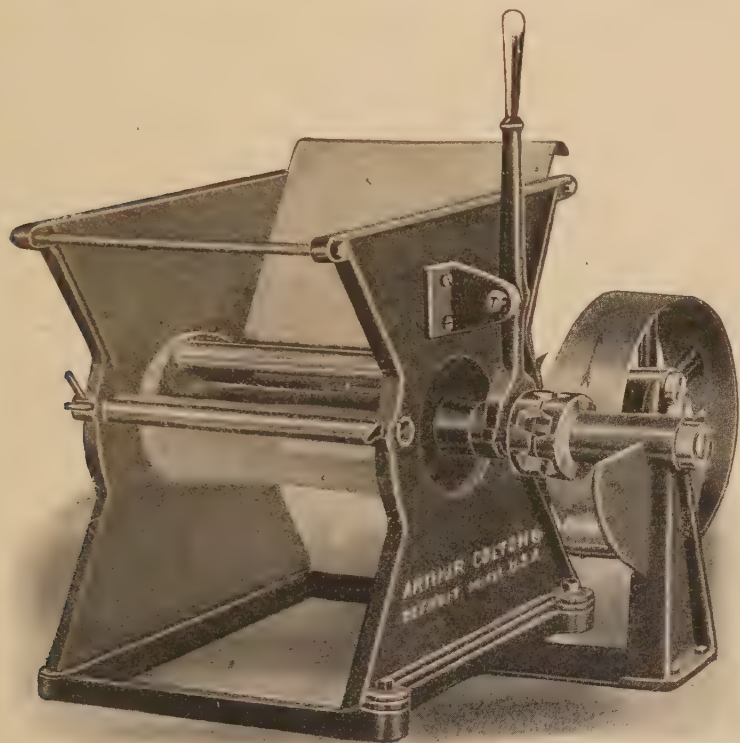


FIG. 30.—Sifter and granulator.

is gradually reduced until the air in contact with the granules is quite dry before the temperature is raised. In this way even drying throughout the granules is secured.

Separate granulation is often needed when chemicals are combined which would react if moistened in contact with each other. For instance calomel and sodium bicarbonate, if mixed and the mixture moistened to granulate it, will discolor by reason of a partial reaction. The calomel and the sodium bicarbonate must be granulated separately and the granules thoroughly mixed after drying. This is a common

procedure in making tablets containing several ingredients. Incompatibilities must be foreseen and avoided in this way.

Other troublesome combinations are those in which two ingredients form a soft mass, or possibly a liquid, when mixed. If this tendency is very marked, satisfactory tablets cannot be made. When the proportion of one ingredient is very small it can sometimes be added to the granulation, but not granulated in with the reacting ingredients.

Fine powders may be mixed with granular material in very small proportions, but this procedure is better avoided. Fine powders separate from the granulation and thus cause uneven dosage, and they also cause chipping in the tablets. Two good reasons for avoiding the practice.

Success in tablet-making depends in large measure upon the condition of the material, and too much care cannot be exercised in securing a proper granulation.

To prevent the tablet material from sticking to the machine when compressed, some lubricant may be necessary. Many substances compress well without any lubricant, but hygroscopic substances are often troublesome in this regard. Much depends upon the dryness of the material. If the granules are left slightly moist they will stick to the machine, and a further drying may remedy this.

The lubricants commonly used are liquid petrolatum, talcum and boric acid. The first must be used very sparingly, especially on soluble tablets, a drachm to a pound of material being the usual limit. It is best applied dissolved in about 50 parts of ether, and is sprayed on from an atomizer, then the powder is spread out and the ether allowed to evaporate. Vaseline or petrolatum may be employed in place of the liquid oil. But if either be used too freely the oil will show when the tablet is dropped into water. In cases when ether would soften or dissolve the material, the lubricant is applied without dilution, being added to a portion of the powder, and when well distributed through, this is mixed with the rest. Oil is especially needed when tablets stick at the edges.

If the oil is not sufficient in the above proportion, a little talcum may be added. Talcum is objectionable for tablets which are intended to be dissolved, because it makes a cloudy solution, but it is effective and is employed in troublesome cases in spite of its insolubility. As much as a grain per tablet has been employed. It is, of course, advisable to use as little as will do the work.

Boric acid is preferred for soluble tablets because it is soluble. It is not so effective as talcum, and must either be used in larger proportion, or be combined with talcum. As a rule combinations of talcum and boric acid are better than the latter alone, except in cases of hypodermic tablets where a crystal-clear solution is necessary.

Lycopodium may also be used for colored tablets, but its use is very limited.

The rule has been made that not more than 3 per cent of talcum or 2 per cent. of boric acid, or 1 per cent of lycopodium should be used. This rule will apply in many cases, but all rules have their exceptions. Powder-lubricants produce their best effects when the surface of the tablet is inclined to stick to the dies. The most sparing use of lubricants is always in order, and it will be found that a thorough distribu-

tion of a small quantity will do quite as much good as a large quantity imperfectly mixed.

In adding lubricants, be careful not to break the granules. The granulated material is put upon a large sheet of paper, or in a dish, the lubricant sprinkled upon it and then worked in by means of a spatula or wooden shovel.

Cacao Butter.—An English pharmacist, Mr. E. White, has suggested cacao butter to serve the double purpose of a granulating and lubricating material. The powders are granulated by mixing with cacao butter under proper conditions, then compressing.

He suggested first a mixture of one part of cacao butter and three parts of starch, this to be mixed with the powder in the proportion of 1 part of excipient to 3 to 5 parts of powder, preferably warm. Later an emulsion of cacao butter was recommended, made by dissolving 5 parts of soap or acacia in 25 parts of *hot* water, and adding 25 parts of melted cacao butter. This is well shaken until the butter is emulsified, then 0.5 part of powdered tragacanth and 0.5 part of benzoic acid are added and well shaken in. Finally enough warm water is added to make the whole weigh 100 parts, and the agitation continued until the mixture is creamy. This emulsion is added to the material previously mixed with 5 to 10 per cent. of sugar in the proportion of 1 part of emulsion to 5 to 7 parts of powder. The mixture is rubbed through a coarse sieve, dried without heat, again sifted, and then compressed.

For substances which are very soluble in water, as opium, aloë, pepsin, vegetable extracts, etc., a solution of cacao butter in ether and alcohol is better. This is made by dissolving 1 part of the butter in 5 parts of ether, and mixing this solution with an equal volume of alcohol at the time of use. This is employed in the same manner and proportions as the butter.

Dr. Fantus has applied the same principle in a different form by recommending a mixture of 25 parts of liquid petrolatum and 75 parts of starch as a granulating material. This is mixed with the medicinal agent in proportion of 1 to 30 per cent of the mixture for extemporaneous tablets. For most mixtures 20 per cent. of the starch mixture he states gives the best results. This is just enough to impart a granular character without making the mixture sticky or greasy. Do not triturate hard.

Powdered cocoa is a natural mixture of fat with vegetable matter which acts in the same manner, and in addition is a good flavoring agent. The cocoa should contain about 25 per cent of cacao butter to serve well.

Tablets made with cacao butter are usually a little colored, and unless care is taken in the mixing they may be spotted. They are not as hard as tablets which have been granulated with syrup, and in the author's experience the butter is not always a success as a lubricant.

The difficulty appears to be that the cold butter fails to act well as a lubricant, and the tablets lack smoothness. It also lacks adhesiveness when cold, and more pressure is necessary, but the tablets still crumble easily. Since the method requires quite as much time as the older method of granulating and subsequent lubrication, its advantages are not apparent.

To secure soluble or medicinally active tablets, the tablet must either dissolve readily in water, or fall into a powder shortly after being dropped into water. The solubility of the tablet will depend, after the question of the solubility of its ingredients, upon its hardness, and upon a sparing use of lubricants. A very hard tablet will dissolve slowly, and an excess of oil in the tablet will hinder solution.

For bodies which are insoluble in water, some means of forcing them apart when they are dropped into water is necessary. There are two ways of accomplishing this. First to mix with the insoluble powder a small quantity of a mixture of bicarbonate of sodium and citric or tartaric acid, so that when the tablet is dropped into water an effervescence takes place within the tablet, thus breaking it up and forcing the tablet into powder. This method is preferred in hypodermic tablets, and in cases where a clear solution finally occurs. But a very slight proportion of effervescent material is needed.

For such substances as acetanilid, bismuth subnitrate, and other insoluble chemicals, starch is employed. Starch is a very hygroscopic substance, and absorbs about one-fifth its weight of water in a moist atmosphere without appearing wet. If then starch be dried thoroughly at a temperature of 100° C. it will swell without gelatinizing or dissolving when immersed in cold water. Advantage is taken of this fact to make **disintegrating tablets**. The powder is granulated as usual and dried. Immediately before compressing, starch, recently dried at 100° C., is added so that each tablet will contain 15 to 20 per cent. (or $1\frac{1}{2}$ to 1 grain) of the dry starch. The mixture is then compressed. When these tablets are dropped into water the starch swells immediately and the tablet falls to powder. They must be kept in well-closed containers, or they will gradually absorb enough moisture to prevent disintegration.

This treatment is advisable for tablets of all insoluble materials which do not swell in water. Vegetable powders will, of themselves, gradually swell in water and disintegrate, and additional treatment is not needed for these.

Manipulation in Specific Cases.—It is manifestly impossible to give in detail the directions for making all kinds or combinations of medicinal agents into tablets. As in other forms of medication, a knowledge of the properties of the material, judgment in handling, and some experience is needed to turn out perfect tablets.

The following classification, and the formulas which follow will illustrate the methods of dealing with the various agents, and will suggest the manipulation for others.

Soluble Salts.—These are mostly crystalline, and can be easily secured in a granular condition. If the crystals are too large they may be ground coarsely in a mill, then sifted, to separate any fine powder, and any large crystals which may have escaped the milling. Non-deliquescent salts are then compressed without any further treatment.

Salts which contain much water of crystallization may liquefy under the pressure and thus give trouble. These need to be dried and granulated by means of an excipient.

Non-crystalline soluble salts like bicarbonate of sodium, salicylate of sodium, etc., may be mixed with about 10 per cent. of sugar and

5 per cent. of white dextrin and granulated with diluted alcohol. In mixtures these may require to be granulated by themselves and the granules mixed.

Deliquescent salts are troublesome. They must be well dried before putting into the machine, and if they are very deliquescent, granulation with acacia may be needed. In this case the salt is dried, powdered finely, mixed with one-twentieth or one-fortieth its weight of powdered acacia, moistened with enough water to granulate it, sifted and again dried. As a rule, salts which require this treatment are considered unsuitable for tablet form, and the operation is therefore rarely required. It should also be borne in mind that deliquescent salts may corrode the dies, and the machine needs special protection from them.

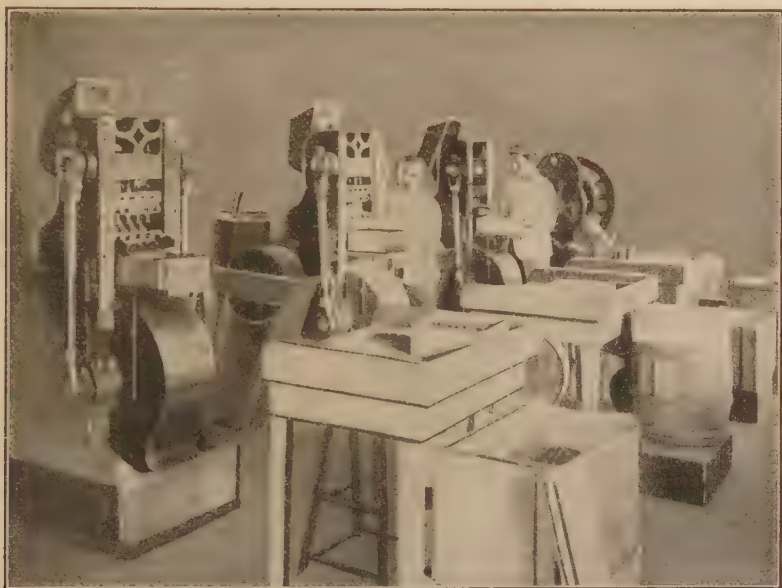


FIG. 31.—Quadruple-die tablet machines for heavy work.

Efflorescent salts, when compressed alone, need only to be in a good granular condition unless the pressure liquefies them. When they are combined, the heavy pressure may start a reaction, and to prevent this they may require to be dried and granulated as other powders. This is necessary only when the pressure needed to form the tablets squeezes out enough water to start the reaction, or to spoil the appearance of the tablet.

Reducible salts, such as silver nitrate, potassium chlorate, potassium permanganate, etc., may be compressed alone but should not be mixed with organic matter. They are crystalline, and offer no difficulties if compressed alone except that especial care is needed to exclude reactive matter. The compression of potassium chlorate or permanganate in which a small amount of organic matter was present has resulted in fire and damage to the machine. If they are to be

diluted, inorganic vehicles as kaolin (for tablets not intended to be dissolved) or dried sodium sulphate, magnesium sulphate, etc. (for soluble tablets), should be used as the diluent.

Incompatible salts when combined in tablets often need to be protected. In combinations like lead acetate and zinc sulphate, wherein the salts contain water of crystallization, the salts must be desiccated

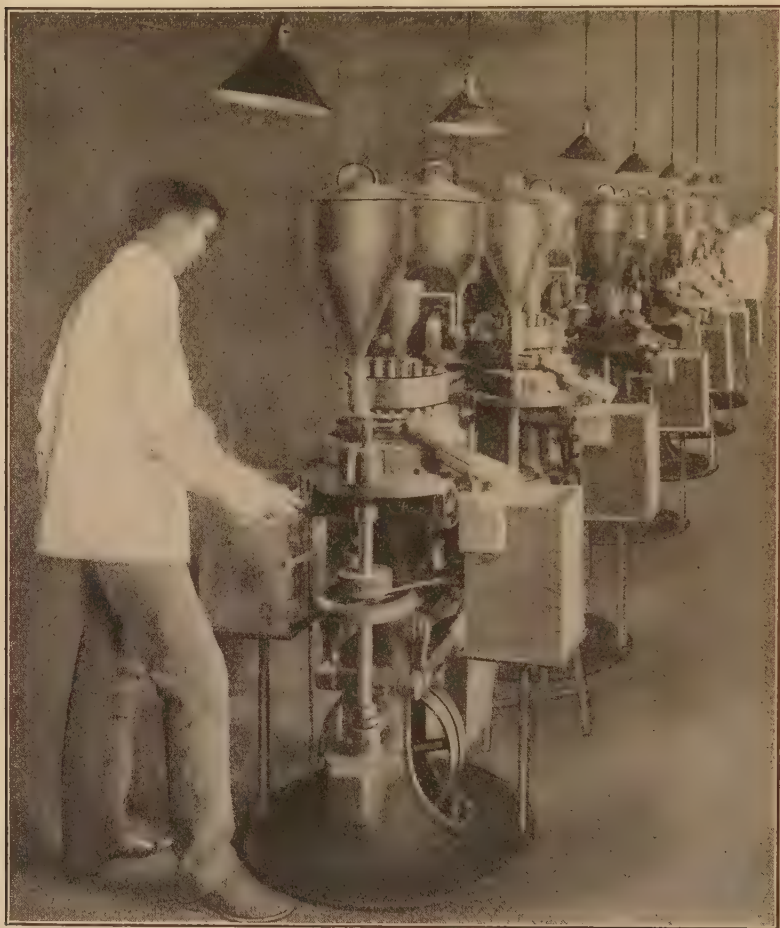


FIG. 32.—Rotary tablet machines. Capacity 500 to 800 tablets per minute.

and granulated separately, else the pressure of the dies will liberate the water of crystallization and produce a pasty mass instead of a smooth tablet.

Effervescing tablets are best made by granulating the alkali and acid separately, the other ingredients being mixed with either, or divided between the two, as is most convenient. It is possible to make these by granulating the complete mixture with alcohol and

drying quickly and thoroughly, but this method requires more skill and care, and good drying facilities. They need special caution in lubricating, since citric and tartaric acid are hygroscopic and tend to stick. The drying is an important factor in these.

Mercury salts are easily reduced by contact with metals when wet, and are liable to be discolored by sifting the damp mass through a metallic sieve. It is better to granulate these by a careful adjustment of the excipient, dry without sifting, then sift when well dried. Unless well dried, the dies may cause a discoloration.

Insoluble Chemicals.—These need more excipient, as a rule, to cause them to granulate and cohere well. Starch paste or gelatin solution are usually the best excipients for this class. Just before compression some freshly dried starch should be distributed through the granules to cause the tablets to disintegrate when dropped into water. One quarter to one grain of dry starch per tablet of 3 to 5 grains is the quantity usually required. If a lubricant is needed it should be added to the granulated material before the starch is mixed in. The compression should be as light as will form a tablet with this class.

Bodies belonging to this class are acetanilid, antipyrin, bismuth salicylate, bismuth subcarbonate, bismuth subnitrate, chloralamid, cinchonidine, phenacetin, quinine sulphate, salicin, salol, sulphonal, sulphur, trional, etc.

Insoluble bodies which are given in very small doses and in dilutions, should be triturated with sugar of milk and the mixture granulated. The sugar of milk is soluble, and being in excess no starch is needed. It forms a better triturating medium than cane sugar. Examples of this class are arsenous acid, calcium sulphide, calomel, mercuric iodide, mercurous iodide, etc.

Some insoluble bodies like naphthalin which are made into tablets for convenience and not intended for internal administration are simply moistened very slightly with water and compressed.

Light and bulky bodies like charcoal, hygroscopic bodies like powdered pepsin, need a larger proportion of sugar to granulate them, and must be formed into fine granules. Charcoal should be mixed with a quarter of its weight of sugar, and granulated with water. Powdered pepsin should be mixed with an eighth to a sixth of its weight of sugar.

The granulated powder should be fine enough to pass through a No. 60 sieve, because the spongy nature of these bodies makes more resistance to compression and the particles do not cohere as well as more compact substances.

Vegetable substances require more liquid to moisten them in granulating, and must either be granulated quickly or considerable time allowed for drying the granules. A little gum is necessary to impart adhesiveness in some cases. Dextrin is to be preferred.

Tinctures, Extracts and Fluid Extracts.—Tinctures, unless used in quantities small enough to allow of their use as moistening agents, must be evaporated to a small bulk and then so used. Frequently an equivalent quantity of the corresponding fluidextract can be substituted for the tincture and evaporation thus avoided. If no other medicinal agent is directed in the tablet, starch, licorice, sugar of milk, or other absorbent body must be employed.

These may also be necessary as adjuncts to other powders in compound tablets. Fluidextracts are treated in the same way as tinctures.

Extracts are softened by trituration with a suitable menstruum to a semifluid consistency, then this is used as the moistening agent. Tablets containing any large proportion of extractive matter may need to be lubricated well to prevent sticking. They also need special care in drying.

Gum resins, oleoresins, resins, etc., may be granulated by grinding coarsely. If the powders are employed they should be moistened very cautiously with alcohol, and dried at a low temperature.

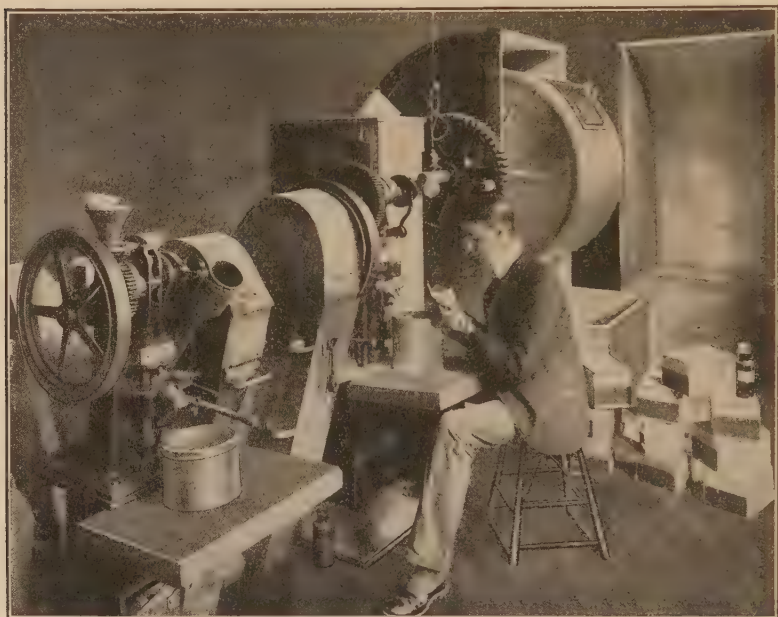


FIG. 33.—Making mercuric chloride tablets. Granulation and compression done in one room.

They need no lubricating agent, and form smooth and firm tablets very easily as a rule.

Volatile oils, etc., must be absorbed in some dry media. They are best distributed through the other material previously granulated. If the oil is in small proportion it may be dissolved in ether before mixing with the granules, then the latter is dried at a low temperature. Oils act as lubricants, and there is usually no need of further lubrication.

Creosote is directed to be absorbed in starch or licorice, allowed to stand for an hour or so, then add sugar and granulate with 75 per cent alcohol. It may also be distributed over the solids previously granulated.

Alkaloids and Potent Principles.—These are usually trituated with sugar of milk for tablets. They present no difficulties, and no

gum is needed. Beside alkaloids such bodies as aloin, podophyllin, digitalin, arsenous acid, etc., are so treated.

Hypodermic Tablets.—These should be made with finely powdered cane sugar, or a mixture of lactose and sucrose, moistened with alcohol to granulate, and thoroughly dried. Lubricate with 1 per cent of boric acid, if necessary, and avoid petrolatum or paraffin oil. Compress as lightly as possible. The usual quantity of sugar employed is one-half grain per tablet.

DIFFICULTIES

The common difficulties in compressed tablet-making are (1) crumbling, (2) chipping, (3) sticking to the dies, (4) discoloration and (5) insolubility.

Crumbling may be due to insufficient pressure, or to a lack of adhesiveness. If from the latter cause, the granules may be too dry or the substance may be deficient in adhesive qualities.

Moistening the granules *very slightly* with water, preferably by spraying with an atomizer, will correct the former. The moistening should be very slight, and not enough to make the granules appear moist. If the substance is insoluble, and dry starch is needed to make the tablets disintegrate, moistening the granules will destroy the disintegrating power of the starch, and the following remedy should be employed.

If crumbling is due to a lack of adhesiveness, this is best remedied by the addition of sugar and gum. The granules may be sprinkled lightly with a mixture of two parts of finely powdered sugar and one of white dextrin. If this does not suffice, regranulation with 10 to 20 per cent of the starch-dextrin mixture or with gelatin solution may be necessary. In very obstinate cases the use of a little acacia, 1 to 3 per cent may be needed, but acacia should be avoided if possible.

Chipping, or the breaking off of a thin film from the surface of the tablet, is usually due to fine powder or to excessive pressure, and is more likely to occur in thick than in thin tablets. All materials are somewhat elastic, and in a thick tablet the surfaces are compressed harder than the center, hence a skin is formed which is harder than the interior of the tablet, and it tends to break away. Diminishing the pressure, or changing the dies (to make a larger-sized tablet) will often remedy this difficulty.

Sticking to the dies is, obviously, due to an excessive stickiness in the material. It is often caused by moisture in the granules, particularly when deliquescent or hygroscopic substances are present. Further drying the granules will help, if not entirely remedy, this difficulty. This is the first remedy to be tried in all such cases.

Lubricants are also needed in the majority of cases. The choice and use of lubricants calls for discrimination. Liquid petrolatum is the most effective. It must be used very sparingly, or it will show in the water in which the tablet is subsequently dropped. Or it may even make a greasy surface on the tablets. A combination of lubricants is needed in very difficult cases. After the limit of oil has failed to prevent sticking, talcum must be added. And if an excessive amount of talcum is also required, boric acid may also be used, particularly for soluble tablets.

All this suggests that sticking is sometimes a very troublesome difficulty. This is the case. But like most difficulties in work, the best remedy lies in beginning right. Proper granulation and drying of the materials will accomplish more than all else in preventing subsequent trouble. Then a judicious choice and use of lubricants will solve all problems. The general rule is talc or boric acid for the surface, and oil for the edge of the tablets.

Liquid petrolatum works best when added last.

Discoloration may be due to imperfect mixing of oily materials or of saccharine substances. It is shown by spots on the surface of the tablets which are irregular and uneven. A more thorough mixing is, of course, the remedy for this.

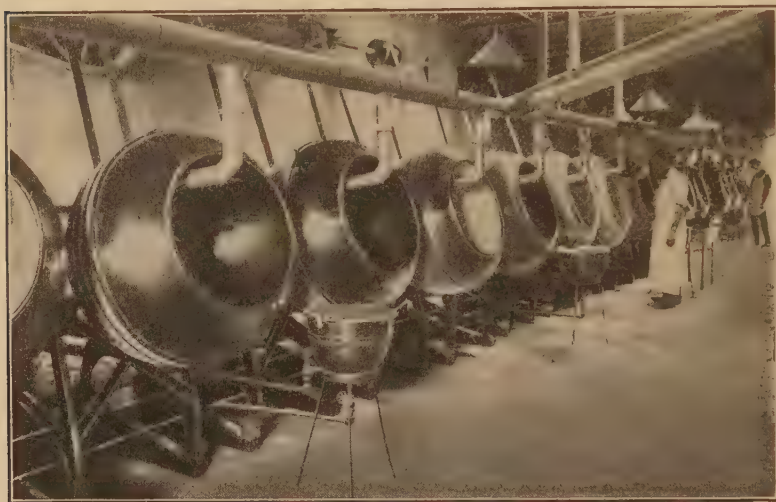


FIG. 34.—Pans for chocolate coating.

Discoloration is also caused by excessive pressure, the oil being squeezed out of oily drugs, or when an oil is an ingredient of the tablet, too much pressure forces it to the surface. Reducing the pressure is the remedy, unless an excessive quantity of oil is present. Then it may be necessary to make a larger tablet, using a vegetable absorbent preferably, to better absorb the oil.

Insolubility or inactivity of tablets depends, of course, more upon the character of the ingredients than upon the condition of the tablets. But since all kinds of substances are incorporated in tablets, and all are expected to be medicinally active, the condition of the tablet must be as favorable to solubility or disintegration as possible.

Too much pressure, an excess of gum, particularly acacia, and excessive lubrication all tend to hinder medicinal activity in the tablet.

If starch is employed as a disintegrating material, it must be thoroughly dry at the time the tablet is made. Otherwise it is useless for this purpose.

TRITURATE TABLETS

Triturate tablets or tablet triturates are made of fine powders in a moist condition. They are an American idea, having been introduced by Dr. Robert Fuller, of Philadelphia.

They are very small and comparatively thick lozenges, differing from troches in being easily crushed, and containing no gum, and from compressed tablets in being diluted medicinal agents, and in being made from very fine powders.

They are especially adapted for the administering of very powerful remedies, or such as are given in very small doses, such as strychnine, morphine, narcotic extracts, etc. They are used either as substitutes for pills, when, if properly made, they act more promptly, or for making solutions. They should quickly dissolve or fall into powder when dropped into water. Most hypodermic tablets are triturate tablets because they dissolve more quickly than compressed tablets. Bulky medicines are seldom adapted to triturate tablets, but tinctures and fluid extracts are sometimes used in this form.

They are made in moulds, consisting of a plate of hard rubber or metal, having the thickness of the desired tablets (usually $\frac{1}{8}$ to $\frac{1}{4}$ inch) and perforated with 50 or 100 holes having the diameter of the tablets. Another plate has a corresponding number of projecting pegs which fit into these holes, and serve to eject the tablets after they are moulded. Each time the mould is filled, 50 or 100 tablets are made.

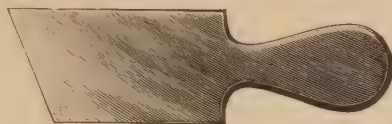


FIG. 35.—Horn spatula for tablet triturates.

In making the tablets, two things are necessary beside the medicinal body and the mould; (1) a suitable diluent, in very fine powder form, and (2) a proper moistening agent.

Diluents.—The term tablet triturates came from the first tablets of this kind which were made from *triturations*, *i. e.*, combinations of potent medicines with sugar of milk, made by trituration, the sugar of milk serving as a diluent. For a time sugar of milk served as the only diluent, but as special qualities in tablets were demanded, other diluents came into use to supply these. The diluents now used are (1) milk sugar, (2) cane sugar, (3) mixtures of milk and cane sugars, and (4) kaolin or precipitated chalk.

The choice of diluent depends upon the character and use of the tablet, and usually is not a matter of great importance. Kaolin or precipitated chalk is only employed for chemicals which would be changed by contact with sugars, such as silver nitrate and potassium permanganate.

Sugar of milk will serve in almost every other case except when a hypodermic tablet is desired, when it is required to dissolve quickly and in a very small quantity of water. Cane sugar is more soluble than milk sugar, and hence makes a more soluble tablet. Aside from

this, cane sugar makes a harder tablet than does milk sugar, and is sometimes preferred for this reason.

The aim in tablets is to get a tablet that will bear handling and the ordinary attrition of bottling without losing any of its form, and yet will crush easily in the fingers. So when milk sugar will make, alone, a tablet which crumbles too easily, a combination of the two sugars will secure a firmer tablet.

Or if cane sugar alone makes too hard a tablet, a small proportion of sugar of milk will prevent hardening, and possibly make a more quickly soluble tablet. So some manufacturers prefer to make most of these tablets from a mixture of five parts of milk sugar with one of cane sugar, as making a harder and less friable tablet than milk sugar alone. And for similar reasons, some prefer to use a mixture of three or four parts of cane sugar with one of milk sugar for hypodermic tablets. But *good tablets* can be made with either sugar alone.

An essential quality in any diluent is that it should be in a very fine and even powder. Nothing coarser than a number 120 powder should be used, and finer powders than this will make smoother tablets. It may be stated as a rule that the finer the powders the smoother the tablets. Tablet manufacturers always sift the diluents before using, to insure this.

Moistening Agents.—The appearance and wearing qualities of the tablets depend, next to the fineness of the diluents, upon the use of the moistening agents. The choice of a moistening agent is comparatively simple—it *should exert a very slight solvent action upon the mixed material of the tablet.*

This is similar to a pill excipient, but for tablets the moistening agent is a thin mobile fluid and need not impart so marked an adhesive or plastic quality as is required in pill excipients.

The moistening agents in common use are (1) alcohol, (2) absolute alcohol, (3) water, (4) mixtures of alcohol and water, and (5) acetone or petroleum benzin and mixtures of these with alcohol.

When the greater bulk of a tablet consists of milk or cane sugar, alcohol serves well as a moistening agent. But if the greater bulk consists of a resinous body, or of an insoluble salt possessing no adhesive quality, or of any substance which is very soluble in alcohol, water is a better moistening agent. In these cases, alcohol would soften the resinous or soluble mass too much, and for the insoluble salt water is needed to develop a full adhesiveness of the sugar and hold the tablet together.

But just as in the ordinary tablet, alcohol tends to make a more friable, and water a harder tablet, so in some instances a mixture of the two strikes a better medium. Mr. Anderson prefers a mixture of 22 parts of alcohol to one of water for moistening most of his tablets. But more care is necessary in using this than for either alone, and the maker who distrusts his skill will be safer with alcohol alone, though his tablets may not wear as well.

Absolute alcohol is only needed for moistening tablets containing very deliquescent bodies, or when water would bring about an undesired reaction, as in a Bland tablet, or when solution of the medicine should be avoided for any reason, as in apomorphine tablets, in which water would develop a green color.

Petroleum benzin is employed for similar purposes as absolute alcohol and for the same reasons. Petroleum benzin alone, or a mixture of this with alcohol (which evaporates more slowly) may be used as a substitute for absolute alcohol.

But more important than the kind, is the amount of the moistening agent to be used. The powders must be thoroughly dampened, but

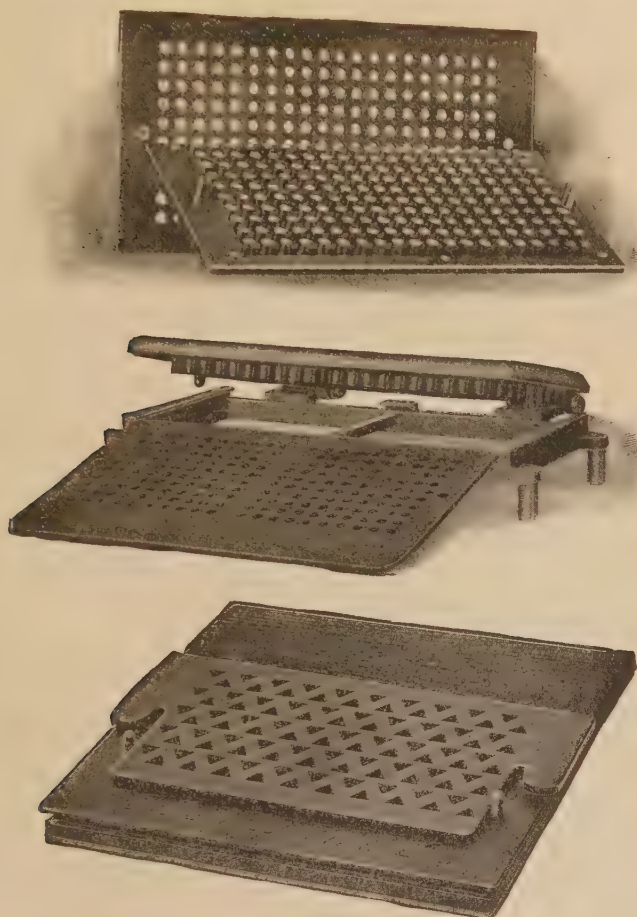


FIG. 36.—Tablet triturate moulds. (Colton.)

must not be pasty. The mass, when pressed into the moulds, must be moist enough to take and hold the form of the moulds, but not enough to show liquid on the surface. The wetter the mass, the more compact and the harder will be the tablets. If not wet enough the tablets will crumble easily.

The mass should be moist enough so that when the moulds are filled, the surface of the tablets will be smooth and free from cracks. On

the other hand, if it is too wet, liquid may show on the surface, and when the tablets are dried they shrink and present a concave surface, or even crack open. An overmoist mass is also likely to stick to the mould, while one moistened just right comes out easily.

In rare instances, when there is too little sugar in the mixture to impart sufficient adhesiveness, and the moistening agents do not act well with the medicinal body, a stiff starch paste has been employed as a moistening agent. This can be used a little more freely than the limpid moistures. Gum solutions should be avoided, as they make too hard a tablet.

In making tablets some calculation, and usually a trial lot, is necessary to insure the accurate quantity of medicinal agent in each tablet. The mould should first be tested, by filling with milk sugar, properly moistened, and the resulting tablets thoroughly dried and weighed. This gives the capacity of the mould in milk sugar alone. It is well to ascertain its capacity in cane sugar also. A trial lot of tablets is then made as follows: The medicinal ingredients are weighed and also the sugar for 50 (or 100) tablets. A portion of the sugar equal in bulk (as accurately as can be judged) to the medicinal ingredients is then set aside, and the rest is mixed, moistened and filled into the mould. If all the holes are filled, and none of the mass is left, by weighing the sugar which was set aside, the amount used can be ascertained and a formula made up for any number of tablets. If there is any mass in excess, it indicates that too much sugar was used, and the excess should be dried, weighed and added to the sugar just set aside, to calculate the quantity which should have been used. If the mould is not completely filled, by counting the unfilled moulds, the additional quantity of sugar needed is readily calculated, and the whole may be re-massed and again tried. Formulas which have been worked out in this way should be recorded for future use.

If a large quantity of one kind of tablets is to be made the triturated mixture should be moistened in portions, only sufficient for a few minutes' filling of the mould being moistened at a time, lest it dry too much.

After the tablets are removed from the mould they must be thoroughly dried. Colored tablets are now liable to become streaked unless dried evenly. A sieve, or a thin cloth stretched upon a frame, should be employed, so that the tablets will dry upon all sides alike. If dried on a hard impervious surface, the upper surface of the tablet will dry first and the color will be deeper there than at the bottom. If only a few tablets are to be made, they may be dried on blotting-paper, which absorbs the moisture from the under surface. All tablets must be thoroughly dried before bottling or they may mould.

When the moulds are filled, both sides should be smoothed off with the spatula, and if the mass is at all sticky, both surfaces should be dusted with a little of the dried mixture, or a suitable dusting-powder before ejecting. Vegetable extracts usually make a sticky mass, and the extract should not exceed one-third the weight of the tablet. It is frequently necessary to dust the moulds with lycopodium or other powder before filling in order to secure smooth tablets. Fluid extracts and tinctures, when not exceeding three-fourths of a minim per grain of mass, can be incorporated as moistening agent

without evaporating. When the quantity exceeds this proportion, they must be evaporated before mixing.

Hypodermic tablets must be moistened as little as possible, in order to secure a porous and friable tablet which will dissolve quickly. A glass plate is the best surface on which to make tablets, and the mould should be slid off rather than lifted up, when filled.

A special tablet spatula of horn, with a very broad and short blade, similar to a putty-knife, is best for filling the moulds. It is more springy than a steel spatula, and it never discolors the tablets.



FIG. 37.—Making hypodermic tablets.

Many commercial tablets which are labeled "tablet triturates" are in reality compressed tablets. The composition of these is essentially the same, and the pressure is the lightest. The reason for making them by compression, is that when the power and machinery are at hand it is cheaper to utilize them in making tablets one at a time, than to let them remain idle while an operator spends his time making tablets 100 at a time. Also that many mixtures are less troublesome to compress in a dry and granular condition than to mould in a moist condition.

Tablet saturates are plain tablets of sugar of milk which are saturated as wanted, with an alcoholic tincture or fluid extract and again dried. These correspond to the homeopathic pellets of sugar which are medicated in the same way. The tablets can be kept in stock,

and medicated at short notice, but they cannot be medicated with aqueous, or weakly alcoholic fluids.

If a tincture is weak in alcohol it will make the tablets sticky and shapeless when poured upon them. The fluid extract of the same drug may be diluted with strong alcohol and used in its place.

Tablet Coating.—Tablets are coated in the same way as pills, except of course that they are never impaled. Flat tablets cannot be coated satisfactorily, hence tablets intended to be coated are made with convex surfaces, and usually the more rounded the surface the easier they are to coat.

The tablets are first rolled in a coating pan to smooth off the edges, then the fine powder is removed by sifting or by an air blast, then the tablets are given a subcoating of suitable material. This subcoating may consist of talcum, clay, calcium carbonate, ferric oxide, starch, chocolate sugar, etc. according to the color and character of the tablet, which is made to adhere in a coating pan by means of syrup or gelatin solution, containing a little gum, if necessary. The tablets are first moistened with the liquid, then the powder is sprinkled on, and the tablets rotated until dry. This process is repeated until a coating of sufficient depth is obtained. The finishing coating, usually consisting of chocolate and sugar, or of sugar with or without coloring, is then put on. The finishing coat must be capable of taking a polish, must be bright and attractive in appearance, and must be pleasant in taste. For coloring, dyes are used which are known to be harmless in character and reasonably permanent in color. Any desired color or shade of color can thus be secured, and we find tablets of all colors in the market. Frequently the same tablet is offered in several shades of color to supply different demands. The color of a coated tablet is therefore no indication of the color of the tablet contents.

The coating of tablets is a more difficult operation than that of pills, hence is less satisfactory on the small scale. For extemporaneous work the same methods as are employed for pills may be tried. But tablet coating is rarely, if ever, demanded at the prescription counter. Dr. R. C. White gives the following formulas for coating (*Jour. Am. Phar. Assoc.*, 1922, p. 345) in connection with a description of coating methods.

Plain Syrup.—40 lbs. granulated sugar in 3 gallons of water.

Chocolate Syrup, Plain.—11 lbs. chocolate paste in 10 gallons of plain syrup.

Heavy Chocolate Syrup.—20 lbs. powdered cocoa and 100 lbs. granulated sugar in 10 gallons plain syrup.

Heavy White Syrup.—20 lbs. coating powder No. 2 and 50 lbs. powdered sugar in 6 gallons plain syrup.

Syrup with Gelatin.—1 lb. powdered acacia, 1 lb. 3 oz. gelatin, 15 lbs. granulated sugar in 13 pints of water.

Syrup with Acacia.—2 lbs. acacia, 15 lbs. granulated sugar in 1 gallon of water.

Coating Powder No. 1, White.—87 lbs. 2 oz. powdered sugar, 12 lbs. 14 oz. powdered acacia. (Practically one part of acacia to 6 $\frac{3}{4}$ parts of sugar.)

Coating Powder No 2.—87 lbs. 8 oz. precipitated chalk, 12 lbs. potato starch. (Practically 7 parts of chalk to 10 of starch.)

Coating Powder No. 3.—14 lbs. 8 oz. fat free cocoa, 2 lbs. 1 oz. powdered extract of licorice, 12 lbs. 7 oz. potato starch, 71 lbs. powdered sugar.

Coating Powder No. 4.—6 1 2 lbs. powdered acacia, 4 1 2 lbs. powdered starch, 88 lbs. powdered sugar.

Polishing Wax.—3 lbs. carnauba wax, 2 lbs. beeswax, 2 lbs. paraffin.

TABLETS

1

Potassium Chlorate

R. Potassium chlorate, granulated..... 200 gr.
Make 100 tablets.

Compress in the machine.

2

Potassium Chlorate and Muriate of Ammonia

R. Potassium chlorate, granulated..... 250 gr.
Ammonium chloride, granulated..... 250 gr.
Make 100 tablets.

Mix thoroughly on paper with a spatula, and compress.

3

Quinine Bisulphate, 2 gr.

R. Quinine bisulphate, crystals, 200 gr.
Make 100 tablets.

Lubricate with paraffin oil; weigh and compress.

4

Ammonium Chloride and Licorice

R. Ammonium chloride, powdered..... 200 gr.
Extract of licorice, powdered..... 800 gr.
Oil of anise..... 5 drops
Make 100 tablets.

Mix the powders, granulate with water, dry, add the oil of anise dissolved in ether, and a little paraffin oil, dry, weigh and compress.

5

Alum Compound

R. Dried alum..... 175 gr.
Zinc sulphate..... 200 gr.
Morphine sulphate..... 4 gr.
Hydrastine muriate..... 4 gr.
Make 100 tablets.

Mix the powders, add 40 gr. of sugar, granulate with syrup, dry, add 5 gr. of boric acid and a little paraffin oil, weigh and compress.

6

Quinine Tablets, 2 gr.

R. Quinine sulphate..... 200 gr.
Make 100 tablets.

Mix the quinine with 20 gr. of sugar and 10 gr. of dextrin, granulate, lubricate with paraffin oil, dry, mix in 25 gr. of dried starch, weigh and compress.

7

Tasteless Quinine, 3 gr.

R. Quinine tannate..... 300 gr.
Powdered chocolate..... 300 gr.
Powdered sugar..... 100 gr.
Saccharin..... 4 gr.
Make 100 tablets.

Mix, granulate with water, lubricate with 25 gr. of talcum, weigh and compress.

8

Phenacetin Tablets, 3 gr.

- R. Phenacetin..... 300 gr.
Make 100 tablets.

Mix the phenacetin, in fine powder, with 30 gr. of sugar and granulate with syrup. Lubricate the dry granules with paraffin oil, shake in 50 gr. of dried starch, and compress.

9

Acetanilid and Soda Tablets

- R. Acetanilid, powdered..... 250 gr.
Sodium bicarbonate..... 250 gr.
Make 100 tablets.

Mix the powders with 50 gr. of powdered sugar and 20 gr. of white dextrin, and granulate. Lubricate the granules with paraffin oil, shake in 25 gr. of dried starch, and compress.

10

Headache Tablets

- R. Acetanilid..... 350 gr.
Sodium bicarbonate..... 100 gr.
Caffeine..... 50 gr.
Make 100 tablets.

Mix with 25 gr. of powdered sugar and 25 gr. of white dextrin, granulate with syrup or water, lubricate with paraffin oil, shake in 40 gr. of dried starch, weigh and compress.

11

Sulphur and Cream of Tartar

- R. Powdered sulphur..... 500 gr.
Cream of tartar..... 500 gr.
Make 100 tablets.

Mix the powders with 50 gr. of powdered sugar and 50 gr. white dextrin, granulate with syrup, dry, add 50 gr. dried starch, weigh and compress.

12

Bismuth and Soda

- R. Bismuth subcarbonate.... 300 gr.
Sodium bicarbonate..... 200 gr.
Make 100 tablets.

Mix with 50 gr. of sugar and 50 gr. of dextrin, granulate, dry, lubricate with paraffin oil, shake in 25 gr. of dried starch and compress.

13

Calomel and Soda

- R. Calomel..... 100 gr.
Sodium bicarbonate..... 100 gr.
Make 100 tablets.

Mix with 20 gr. sugar and 20 gr. of dextrin, granulate, lubricate with paraffin oil, and compress.

14

Iron Quinine and Strychnine

- R. Soluble iron phosphate... 200 gr.
Quinine sulphate..... 100 gr.
Strychnine sulphate..... 1 2/3 gr.
Make 100 tablets.

Mix all with 25 gr. powdered sugar, granulate, lubricate with paraffin oil, and compress.

15

Saccharin

- R. Saccharin..... 10 gr.
Sodium bicarbonate..... 9 gr.
Make 100 tablets.

Mix with 90 gr. sugar of milk and 10 gr. dextrin, granulate and compress.

16

Effervescing Lithia

- R. Lithium citrate..... 300 gr.
Sodium bicarbonate..... 260 gr.
Potassium bicarbonate.... 500 gr.
Citric acid..... 550 gr.
Make 100 tablets.

Mix the bicarbonates with 80 gr. of dextrin, granulate with syrup, and dry well. Mix the acid and lithium citrate, granulate with syrup and dry well. Mix the granules, lubricate with paraffin oil, stir in 100 gr. of talcum, weigh and compress.

17

Effervescing Lithia

- R. Lithium citrate..... 300 gr.
 Sodium bicarbonate..... 300 gr.
 Tartaric acid..... 275 gr.
 Make 100 tablets.

Mix the sodium bicarbonate with 150 gr. sugar and 15 gr. of dextrin, granulate with syrup and dry well. Mix the acid and lithium citrate and granulate with syrup. Mix the granules, lubricate with paraffin oil and talcum, and compress.

18

Soda Mints

- R. Sodium bicarbonate..... 400 gr.
 Oil of peppermint..... 20 min.
 Make 100 tablets.

Granulate the soda with 40 gr. of sugar, and 20 gr. of dextrin, moistening with water. Mix the oil with the dried granules and compress lightly.

19

Rhubarb and Soda

- R. Powdered rhubarb..... 200 gr.
 Sodium bicarbonate..... 200 gr.
 Oil of peppermint..... 11 min.
 Make 100 tablets.

Mix the powders with 50 gr. of sugar and 25 gr. of dextrin, moisten with syrup and granulate. Mix the oil with the dried granules and compress.

20

Opium, 1 Gr.

- R. Powdered opium..... 100 gr.
 Make 100 tablets.

Mix the opium with 25 gr. of sugar granulate with alcohol, dry and compress.

21

Aloe and myrrh

- Aloe..... 200 gr.
 Myrrh..... 100 gr.
 Aromatic powder..... 50 gr.
 Make 100 tablets.

Mix well, granulate with 3/4 alcohol, dry at a low temperature, and compress.

22

Creosote

- R. Creosote..... 100 min.
 Make 100 tablets.

Mix the creosote with 50 gr. of powdered licorice, let stand an hour, add enough sugar to make a granular mass and compress.

23

Dover's Powder

- R. Dover's powder..... 500 gr.
 Make 100 tablets.

Granulate with syrup, dry and compress.

24

Aloin, Strychnine and Belladonna

- R. Aloin..... 60 gr.
 Strychnine..... 1 gr.
 Ext. belladonna..... 15 gr.
 Make 60 tablets.

Mix the aloin and strychnine with 60 gr. of sugar. Soften the extract with diluted alcohol and mix with powders, adding enough water to granulate. Dry at a low temperature, lubricate with paraffin oil and talcum, and compress.

25

Pepsin Tablets

- R. Scale pepsin..... 100 gr.
 Make 100 tablets.

Rub the scales through a No. 30 sieve, lubricate with paraffin oil and compress.

Or, mix 100 gr. of powdered pepsin with 20 gr. of sugar, moisten with diluted alcohol, granulate through a No. 60 sieve, dry, lubricate and compress.

26

Pepsin and Bismuth

- R. Pepsin..... 100 gr.
Bismuth subnitrate..... 500 gr.

Mix with 600 gr. of sugar, granulate with syrup, dry well and lubricate with oil. Shake in 50 gr. of dried starch and compress.

27

Santonin and Calomel

- R. Santonin,
Calomel,
Cocoa,
Sugar..... of each 100 gr.
Make 100 tablets.

Granulate with syrup, and compress.

28

Charcoal, 5 Gr.

- R. Powdered charcoal..... 500 gr.
Make 100 tablets.

Mix with 125 gr. sugar and 25 gr. dextrin, moisten with syrup, granulate through a No. 60 sieve, dry well and compress.

29

Strychnine, 1/60 Gr.

- R. Strychnine sulphate..... 1 2/3 gr.
Sugar of milk..... 100 gr.
Make 100 tablet triturates.

30

Hypodermic Morphine, 1/8 Gr.

- R. Morphine sulphate..... 12 1/2 gr.
Sugar..... 75 gr.
Sugar of milk..... 12 1/2 gr.
Make 100 tablet triturates.

31

Sweet Tablets of Chalk, 2 Gr.

- R. Prepared chalk..... 200 gr.
Cacao butter, white..... 15 gr.
Spirit of cinnamon..... 10 gr.
Solution of carmine..... 2 min.
Powdered sugar..... 285 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

32

Sweet Tablets of Charcoal, 3 Gm.

- R. Charcoal, finely powdered 300 gr.
Paraffin (shaved)..... 15 gr.
Powd. ext. licorice..... 50 gr.
Spirit of anise..... 15 min.
Spirit of coriander..... 8 min.
Powdered sugar..... 135 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

33

Sweet Tablets of Iron Carbonate, Gr. 1/5

- R. Saccharated iron carbonate..... 135 gr.
Paraffin, in thin shavings 15 gr.
Solution of carmine..... 10 min.
Spirit of cinnamon..... 10 min.
Powdered sugar..... 350 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

34

Sweet Tablets of Phenolphthalein, 1 Gr.

- R. Phenolphthalein..... 100 gr.
Chocolate powder..... 50 gr.
Tincture of vanilla..... 15 min.
Alcoholic sol. saccharin,
4 per cent..... 60 min.
Powdered sugar..... 350 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

35

Sweet Tablets of Calomel, 1/10 Gr.

- R. Calomel..... 10 gr.
Paraffin in thin shavings 9 gr.
Talcum..... 9 gr.
Solution of carmine..... 2 min.
Spirit of rose, 10 per cent 5 min.
Powdered sugar..... 272 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

36

Sweet Tablets of Terpin Hydrate, 1/2 Gr.

- R. Terpin hydrate..... 50 gr.
Cacao butter..... 15 gr.
Tincture of curcuma..... 60 min.
Spirit of rose, 10 per cent 5 min.
Powdered sugar..... 435 gr.
Mix and compress into 100 tablets.
(Dr. Fantus.)

State Board Prescriptions

1

2

R Hydrazuri tannatis..... 0.01
 Ft. tabellæ no. xxiv.
 Sig.—Caput unam pro re nata. (N.Y.)

R. Potassii chloratis..... 2.5
 Ext. glycyrrhizæ..... 2.5
 Olei anisi..... gr. x
 M. Ft. trochisci numero duodecim
 consperge.
 Sig.—Caput unam onni quinta hora
 more dicto.

CHAPTER XI

POWDERS, SPECIES, CACHETS, CAPSULES, WAFERS

Species (Lat. *specie-um*).—Very coarsely powdered or merely bruised drugs, intended for the domestic preparation of infusions or decoctions. They are also called “teas,” or “breast-tea,” “physic-tea,” etc.

Powders (Lat. *pulvis-eris*, plural *pulver-es-um*).—Applied to drugs and chemicals administered in the dry powdered form. When divided into doses powders are administered as—

Papers (Lat. *chartulæ-arum*).—Small folded papers each containing a single dose.

Capsules (Lat. *capsulæ-arum*).—Ovoid, or short cylindrical, shells of gelatin usually in two close-fitting parts, in which powders, pastes, or liquids are enclosed.

Cachets (Lat. *capsulæ amylaceæ*).—

Small concavo-convex discs made of flour or starch and gum, the two parts of which, when fitted together and cemented by moistening, form a receptacle for powders. When swallowed, they are softened by dipping into water.

Wafers (Lat. *chartulæ amylaceæ*).—

Small sheets resembling powder-papers, composed of flour or starch and gum, in which, after moistening, powders are folded in the same manner as in papers. These are softened before being swallowed by dipping into water.

Saccelli (*Saccelli amylicci*) differ from wafers only in that they are already folded into an envelope form. The powders are poured into them and they are then sealed by moistening, in the same way as wafers.

The effect of certain medicines upon the system is due to a considerable extent to the form in which they are administered.

If a teaspoonful of dry salt (sodium chloride) be placed upon the tongue and slowly swallowed, it checks hemorrhage of the lungs; but the same amount of salt dissolved in a teacupful of warm water is a prompt emetic.

The alkaline bromides, given in dilute solution, allay excitement, but if swallowed dry they irritate the stomach and anything but a quieting effect is produced.

Bismuth salts owe their efficiency in a measure to mechanical action, and are more often administered in powder form or in mixtures than in solution.

Hence the administration of medicines in powder form is not only a matter of convenience to the patient, or because of insolubility, but oftentimes because of certain peculiar actions upon the system. The bodies which are most frequently prescribed in powders are those which are insoluble in the ordinary solvents, and are too bulky for administration in pills, or when a greater diffusion is desired than can be obtained in pills or tablets.

Thorough diffusion of some drugs and chemicals seems to modify and increase their action. This is illustrated in the official Dover's powder.

The prolonged trituration which is necessary to reduce the coarsely powdered sugar of milk to a fine powder, comminutes and thoroughly

diffuses the ipecac and opium, and the resulting mixture possesses materially different medicinal properties from a corresponding mixture, the ingredients of which are mixed in a crude or "easy" way. Calomel is another of those bodies which act the better the more finely it is powdered, and (within certain limits) the more thoroughly it is diffused.

Such bodies should always be triturated in a mortar.

The dispensing of prescriptions calling for powders, then, demands some knowledge of the therapeutic action of drugs and their physical characteristics, in order to intelligently interpret the physician's desires.

Less observation of incompatibilities is demanded than in most other forms of medication, since chemicals do not readily react in the absence of moisture, and many salts may be administered commingled in powders which could not be combined in liquids or moist solids.

Powders are mixed in three ways: by trituration in a mortar, by stirring with a spatula on paper, and by sifting.

The choice of methods should not be altogether a matter of convenience, but should be governed by the results.

The mortar method is better when pulverization and thorough diffusion is desired, but it gives a more compact powder than sifting.

Light powders, snuffs, insufflations, etc., are best mixed by sifting, thus the powder is not compacted and diffuses more readily when thrown into water or in the air. Powders containing magnesia are most conveniently mixed on a sheet of smooth paper, or by sifting. If triturated heavily in a mortar it is pressed into a heavier condition, and subsequent sifting does not restore its lightness.

Most vegetable and non-crystalline bodies can be mixed by sifting, and the resulting powder diffuses through water more readily than when they are triturated. The sifting should be repeated two or three times, to insure complete admixture, unless combined with stirring on a piece of paper.

A cheap and handy little sieve for mixing small quantities of powders can be constructed from a four-ounce chip ointment box and a small bit of cheese- or bolting-cloth. The top-piece of the cover is removed, leaving only the rim. The cloth is now stretched over the top of the open box and the cover-rim placed in position, so as to hold the cloth in place and leave a part of the rim above. Powders are readily rubbed through the cloth by means of a spatula, and caught inside the box, preferably upon a paper lining, or the bottom of the box may also be removed and the sifted powder caught upon clean paper.

Crystalline salts, even if already powdered, are best mixed by trituration. Wedgwood mortars grow very smooth with use, when powders do not mix as readily in them. A suitable degree of roughness should be occasionally imparted by triturating a little coarse emery in the mortar. Pumice stone, sand, etc., may be used in place of emery, but they are not as quickly effective.

Some bodies, as chloretone and salol, electrify and stick or fly when rubbed. This can be prevented by moistening very slightly with an oil.



FIG. 38.—
Prescription
sieve.

Salts which contain much water of crystallization, such as alum, sodium phosphate, sodium sulphate, etc., may need to be dried before mixing, to prevent reactions.

When small quantities of powerful remedies are to be mixed with bulky powders, the potent drug is first placed in the mortar with an equal bulk of its diluent and triturated until well mixed, then a double volume more of diluent is added and mixed before a further quantity is added, so continuing till the end.

In this way completed admixture is assured with a minimum of time and labor, and the dispenser can always feel confident of the homogeneity of the powder.

If the entire amount of diluting-powder is added to the potent drug at once, even a long-continued trituration will not bring this same confidence.



FIG. 39.—Powder spatula.

When heavy powders are to be mixed with light ones, the mixing is hastened by placing the heavy powder (when first weighed) on top of the lighter; then upon stirring the heavier powder gradually sinks through the lighter and mixes with it in the process. If placed at the bottom of the mortar or sieve, the entire mixing must be done by mechanical force.

Incompatible salts and those containing water should be mixed lightly, as pressure may start a reaction.

Soluble powders may be dispensed in granular condition or powdered. They are easier divided when in powder.

The following suggestions by Mr. Peter Boa,¹ on the effects of different methods of mixing powders, may be found useful. He says: "Certain powders when mixed together are very difficult to diffuse in water, though it may happen that each one by itself can be mixed with ease. Again, there are compound powders in which one or more of the ingredients might be immiscible separately, yet when in combination they do not present the same difficulty. The most marked examples of the peculiarities occur when insoluble, inorganic substances are mixed with vegetable powders. The inorganic substances may be diffusible or non-diffusible, and magnesia and sulphur may be taken as types.

"Sulphur does not diffuse in water by itself, but in combination with vegetable powders it may do so with little difficulty.

"Magnesia diffuses readily, but when compounded with certain vegetable powders it forms a powder which persistently floats upon water. Sulphur has, therefore, to be made miscible; magnesia has to be prevented from becoming immiscible. And it is here that the method of mixing may be brought into play, so as to effect the different results which we have in view."

The magnesia is prevented from becoming immiscible by avoiding trituration, hence we mix magnesia powders on paper or by

¹Phar. Journ. and Trans., 1881, p. 546.

sifting. Sulphur is made miscible by trituration with vegetable powders in a mortar. In cases where both enter into a compound powder, the sulphur may be triturated with vegetable powders, then this mixture combined with the magnesia by sifting or by means of a spatula.

Sometimes, however, magnesia renders resinous and other bodies which are immiscible with water, more diffusible by trituration with them, and no hard and fast rule can be laid down.

DISPENSING POWDERS

Powders are dispensed in bulk; in papers (*chartulae*), in capsules, in cachets, or in wafers.

Powders which are taken in relatively large doses, as a teaspoonful at a time, are dispensed in bulk. If not easily altered by contact with the air, they are placed in a suitable box, which is labelled; but hygroscopic, or changeable powders, granular effervescing salts, etc., should always be dispensed in wide-mouthed bottles.

Sometimes powders which are administered in comparatively small doses are ordered undivided, with the insertion of a sample dose in a separate paper. If a chemical, it should be powdered to destroy its physical identity, and the sample is then carefully weighed, folded in paper in the usual manner, and placed in an envelope plainly marked. This method of dispensing is practiced only in the interests of economy, and is usually eschewed.

Finely powdered drugs should never be used in preparing species, because they make a muddy and disagreeable infusion. The drug should never be finer than a number twenty powder, and in many cases a bruised drug is preferable even to this. The bruising is readily done in an iron mortar. The mixing need not be thorough unless the package is to be divided for the preparation of successive lots of infusion.

Powders which are to be encased in capsules, wafers and cachets are to be first divided in the usual way. The administration of powders in this form is chiefly for the purpose of disguising the taste, but some protection is also afforded against the action of the air.

The action of air and light upon chemical substances calls for special attention in the dispensing of powders, to avoid undesirable changes in their preparation or subsequently. A list of these is given in the following tables, the most important to be memorized being printed in heavy type.

Salts that absorb moisture from damp air and ultimately become liquid, or
DELIQUESCENT SALTS

Acid Carbolic.

“ **Chromic.**

Aluminum Acetate.

“ **Chloride, Bromide and Iodide.**

Ammonium Nitrate.

“ **Valerate.**

Antimony Chloride.

Salts that lose moisture in warm and dry air and become pulverulent, or
EFFLORESCENT SALTS

Acid, Citric.

Barium Acetate.

DELIQUESCENT SALTS	EFFLORESCENT SALTS
Calcium Chloride, Bromide and Iodide.	Calcium Acetate.
“ Chlorate.	Cinchonidine Sulphate.
Cobalt Acetate.	Cobalt Sulphate.
“ Chloride.	Codeine.
“ Nitrate.	Copper Acetate.
Copper Chloride.	“ Sulphate.
“ Nitrate.	
Gold Chloride.	Ferrous Sulphate.
Ferrous Chloride, Bromide and Iodide.	Ferrie Alum (Ferri et Ammonii Sulphas).
Ferric Chloride.	
Hyoscyamine Hydrochloride.	
“ Sulphate.	
Lithium Chloride, Bromide and Iodide.	Lead Acetate.
“ Citrate.	
“ Salicylate.	Magnesium Sulphate.
Magnesium Chloride, Bromide and Iodide.	
Magnesium Acetate.	
“ Chlorate.	Manganese Sulphate.
Manganese Chloride, Bromide and Iodide.	
Manganese Nitrate.	
Physostigmine (Eserine) Sulphate.	
Pilocarpine Hydrochloride.	
Platinum Chloride.	
Potassium Acetate.	Potassium Ferrocyanide.
“ Carbonate.	Potass. & Sod. Tart. (Rochelle Salt).
“ Citrate.	
“ Cyanide.	
“ Hydroxide.	Quinine Bisulphate.
“ Hypophosphite.	“ Hydrochloride.
“ Sulphite.	“ Hydrobromide.
“ Sulphocarbonate.	“ Sulphate.
“ Sulphocyanide.	
“ Tartrate.	
Sodium Hydroxide.	Sodium Acetate.
Sodium Hypophosphite.	“ Arsenate.
“ Iodide.	“ Borate (in warm and dry air).
“ Nitrate.	“ Carbonate.
“ Nitrite.	“ Hyposulphite (above 33° C.).
“ Sulphovinate.	“ Phosphate.
“ Valerate.	“ Pyrophosphate.
	“ Santoninate.
	“ Sulphate.
	“ Sulphite.
	“ Sulphocarbonate.
Strontium Chloride, Bromide and Iodide.	Strontium Acetate.
	“ Nitrate.
Zinc Chloride, Bromide and Iodide.	Strychnine Sulphate.
“ Chlorate.	Zinc Acetate.
“ Nitrate.	“ Sulphate.

Some bodies are **hygroscopic**, *i. e.*, absorb moisture from the damp air, but do not liquefy. Among these are—

Ammonium Chloride, Bromide and Iodide; the first very slightly so, the last badly.

Amylene Hydrate.

Chloral and Butyl Chloral, Chlorinated Lime (very hygroscopic).

Dried Alum, Dried Sulphate of Iron, Dried Carbonate of Sodium, and other exsiccated salts.

Granular Effervescing Salts.

Citrate of Iron, Phosphate of Iron, and Pyrophosphate of Iron (in scale form).

Saccharated Iodide of Iron (very hygroscopic).

Pepsin (very hygroscopic).

Sulphuretted Potassa.

Sodium Chloride (slightly), and Bromide.

Sparteine Sulphate.

Other bodies are decomposed, volatilized, or become changed in color and appearance when exposed freely to the action of air and light. Care should be exercised in dispensing such to see that they are in proper condition, and to prevent any subsequent change.

SUBSTANCE	CHARACTER OF CHANGE	REMARKS
Acid, Benzoic.....	Darkens.....	By action of strong light.
" Carbolic.....	Becomes red.....	No deterioration in value.
Adrenalin.....	Darkens.....	Shows decomposition.
Ammonium Benzoate..	Loses NH_3	Restored by addition of ammonia water.
" Bromide...	Decomposes.....	" " "
" Carbonate	".....	Loses both NH_3 and CO_2 and finally becomes bicarbonate.
" Iodide.....	".....	Restored by addition of ammonium sulphide or by washing with ether.
" Valerate...	".....	Restored by addition of ammonia water.
Apomorphine Hydrochlorate.....	Becomes greenish....	By action of light, rapidly.
Aconitine.....	" yellowish....	" " "
Aristol.....	Decomposes.....	" "
Arsenic Iodide.....	Loses iodine.....	Decomposes very easily.
Bismuth and Ammonium Citrate	Loses NH_3	Restored by addition of ammonia water.
Calcium Hypophosphite	Oxidizes.....	By action of air.
" Sulphide.....	".....	" " "
Camphor.....	Evaporates.....	
Chinoline.....	Decomposes.....	
Chloral.....	Volatilizes and becomes acid.....	
Chrysarobin.....	Darkens.....	By action of light.
Cinchonidine Salts....	Become brownish....	Very slowly by action of light.
Cinchonine Salts.....	" ".....	" " "
Euophen.....	Decomposes.....	
Ferrous Carbonate, saccharated.....	Oxidizes and darkens.	By action of air; best kept in the light.
Ferrous Iodide, saccharated.....	" ".....	" " "
Ferrous Salts in general	" ".....	" " "
Ferric, scale salts.....	Darken.....	Become less soluble, by action of light.
Iodides in general.....	Partially decompose	By action of light and air.
Iodoform.....	Darkens.....	Loses iodine and volatilizes.
Lead Acetate.....	Loses acetic acid.	Restored by addition of acetic acid.

SUBSTANCE	CHARACTER OF CHANGE	REMARKS
Lime.....	Absorbs water, and carbonates.....	Must be kept in tight containers.
Lime, chlorinated.....	Absorbs water and loses chlorine.....	" " " "
Magnesium Sulphite....	Oxidizes.....	By action of air.
Mercuric Cyanide.....	Darkens.....	By action of light.
" Iodide.....	Reduced, darkens....	By action of strong light.
Mercurous Chloride.....	" ".....	" " " "
" Iodide.....	" ".....	Reduced rapidly by light, forming metallic mercury and poisonous red iodide.
Mercuric Oxide, yellow	" ".....	By action of light.
" " red.....	" ".....	" " " very slowly.
Morphine Acetate.....	Loses acetic acid.....	
Potassa, sulphurated....	Oxidizes.....	By action of air.
Potassium Cyanide.....	Loses CN, and carbonates.....	By action of air
" Hypophosphite.....	Oxidizes.....	" " more rapidly if deliquesced.
Pyrogallol.....	Oxidizes and darkens	By action of air and light.
Quinine Salts.....	Become brownish....	" light very slowly.
Resorcin.....	Darkens.....	" air and light.
Santonin.....	Becomes yellowish....	" light.
Silver Salts, all.....	Reduced and darken	Must be well protected from light and organic matter.
Sodium Santoninate....	Becomes yellowish....	By action of light.
" Bicarbonate.....	Loses CO ₂ —reduced to carbonate.....	By warm air.
" Bisulphite.....	Loses sulphurous acid	By action of air.
" Salicylate.....	Darkens.....	" strong light, in presence of alkalies.
" Sulphite.....	Oxidizes to sulphate	By action of air.
Sulphur Iodide.....	Loses iodine.....	" "
Zinc Acetate.....	Loses acetic acid.....	Restored by addition of acetic acid.
" Iodide.....	Oxidizes and liberates iodine.....	By action of air.
" Phosphide.....	Emits phosphorous vapor.....	" "
" Valerate.....	Loses valeric acid....	Restored by addition of valeric acid.

Eutectic Mixtures.—When phenols or phenolic compounds, aldehyd compounds and ketonic bodies are mixed, the mixture may have a melting-point considerably below that of any of the individual ingredients. This is analogous to the alloys, and the term eutectic applies specifically to the proportions which will produce the lowest melting-point.

Thus a mixture of one part of thymol (melting at 48° to 51° C.) with two parts of acetanilid (melting at 113° C.) will melt at 18.5° C., or be liquid at ordinary temperatures. Mixtures in other proportions may melt below 40, but may be either dry or pasty or fluid at ordinary temperatures.

R. J. Wotring says that a mixture of one part of salol (melting-point 42°) with two of menthol (melting-point 43°) is a dry powder at ordinary temperatures, but if the proportions be reversed and two

parts of salol be mixed with one of menthol a liquid results. This means that the latter proportions come nearer to the true eutectic point, and the melting-point is below the ordinary temperature of the room. But if the first mixture be warmed, it also will liquefy.

Again, a mixture of nine parts of salol with one of betanaphthol will melt at 34.5°C . or of nine of salol with one of phenacetine at 32° , and such mixtures will be either dry or pasty at ordinary temperatures but easily liquefied by warming.

Since the use of synthetic remedies has become common, such mixtures are very frequently prescribed, and are a source of considerable trouble in powder and capsule compounding.

It is obviously impracticable to predict in all cases what is likely to result from any given mixture, and the problem is complicated by the fact that a third body may cause liquefaction when two do not. Thus salol mixes well with either antipyrin or resorcin, forming a dry powder, but if all three are mixed anything from a liquid to a pasty mass may be expected, according to proportions. Likewise salol and acetanilid makes a dry mixture, but add antipyrin and a liquid results. (Wotring.)

The number of such mixtures that are prescribed is large, and applies particularly to the newer remedies, as acetanilid, betanaphthol, antipyrine, phenacetine, salol, camphor, menthol, thymol, chloral, resorcinol, sulphonal, trional, salicylic acid and salicylates, etc. Some of these eutectic combinations are mentioned in the chapter on Incompatibilities under the respective subjects, but the possible combinations are legion and the compounder must constantly be on his guard.

Some warning may come to mind from considering the chemical nature of the ingredients, and if one is well posted on the "phase rule" eutectics may often be predicted, but few pharmacists are posted in the higher branches of chemical physics.

The problem in pharmacy is to find the best treatment when such mixtures are ordered, and must be dispensed.

If a liquid will result, the mixture is not suitable for powders, but may often be made into a mass and dispensed in capsules.

When the resulting mixture is only damp or pasty, the addition of dry starch or (whenever compatible) magnesia will absorb the moisture and allow of dispensing in powders. Starch which has been dried at 100°C . and kept in tightly stoppered bottles has considerable absorptive power and is much more efficient than air-dry starch.

It is well also to avoid rubbing such mixtures together. Mix lightly and liquefaction is less liable to occur. Sometimes the order of mixing makes a material difference, but usually starch or some other absorbent powder is needed.

GRANULAR EFFERVESCING SALTS

These may be easily and quickly made, to satisfy small special orders, at the prescription counter. The basis of these is a mixture of sodium bicarbonate with citric or tartaric acid and may or may not contain sugar.

When thrown into water the bicarbonate is neutralized, carbonic acid is evolved, causing the effervescence, and a citrate or tartrate

of sodium remains in solution, a slight excess of acid usually being present to give a pleasant acidulous taste.

Citric acid mixtures are easier to granulate than tartaric mixtures, but the latter are less expensive, and are frequently employed for that reason, but usually in conjunction with the citric.

The bicarbonate and acid are used in nearly molecular proportions, *i. e.*, 84 parts of sodium bicarbonate to 70 parts of citric acid or 75 parts of tartaric acid. The amount of sugar varies with different mixtures, and may be made to serve as a filling.

All these salts are given in teaspoonful (or multiples of it) doses, and 90 grains (6 Gm.) of finished salt are reckoned as a teaspoonful. Then if 10 grains of a salt are desired at a dose, the mixture which is to be granulated consists of 80 grains of effervescing mixture (with sugar) and 10 grains of medicament.

Since each 90 grains represents one teaspoonful, or ordinary dose, 20 teaspoonfuls would weigh 1,800 grains, or a little less than 4 troy-ounces, which is a convenient quantity to operate upon.

In this quantity 600 grains of sodium bicarbonate may be used with 500 grains of citric acid or 540 grains of tartaric acid. To these amounts are added 5 times 20 grains, or 10 times 20 grains or 20 times 20 grains, as the case may be, of the active medicinal ingredient and enough sugar to make the whole weigh 1,800 grains.

Thus a granulated effervescing potassium bromide, containing 5 grains to the teaspoonful, would require 600 grains of sodium bicarbonate, 540 grains of tartaric acid, 5×20 grains = 100 grains of potassium bromide, and $1,800 - (600 + 540 + 100) = 560$ grains of sugar.

Professor G. A. Bergy recommends that the calculations be made first on a single dose basis. Thus 90 grains (or 6 Gm.) of an effervescing mixture containing 10 grains per dose of a medicament, will call for 80 grains of the effervescent base. If unsweetened this will call for 54.54 per cent or 43.6 grains of sodium bicarbonate, and 45.45 percent, or 36.4 grains of citric acid. If the saline be sweetened, then we may arbitrarily use 35 grains of powdered sugar and for the remaining 53 grains use 30 grains of sodium bicarbonate and 25 grains of citric acid (or 27 grains of tartaric acid). In common fractions the proportion is practically $\frac{1}{3}$ of sodium bicarbonate and $\frac{1}{3}$ of citric acid.

In a few cases it might be advisable to vary the proportions of soda-acid mixture to sugar, but the above will give quite satisfactory results in a large number of cases. A good idea of the varieties may be obtained from a comparative study of the formulas for effervescing salts in the Pharmacopœia and National Formulary.

Since sugar tends to discolor the salt when granulating it is now used much less than formerly, and the total mixture is made up with the acid-bicarbonate mixture alone. If sweetening is desired a little saccharin is used.

Granulation may be effected in two ways, by means of heat or by moistening.

When sugar and tartaric or citric acids are heated they become soft and sticky, as though moistened. In these mixtures a heat of about 200° F.—a little below that of the water-bath—is required to produce large and even granules. Direct flame should not be

used, lest the mixture be burned, and become discolored. A glycerin or paraffin bath will give better results.

The powdered mixture is placed in a tinned-iron or porcelain dish, and heated until it becomes sticky, then it must be kneaded vigorously with a wooden spatula (do not use steel) or a tinned-iron spoon until the entire mass is well granulated, when the mixture is removed from the heat and the stirring continued until cool. In the warm and moist mass a reaction begins between the acid and the bicarbonate present, and a little water is liberated, which aids the granulation. But care must be taken to thoroughly dry the granules before putting into



FIG. 40.—Granular effervescent salts manufacturing.

bottles, or the mixture will gradually become damp and lose its effervescent properties. Mixtures containing bromides are liable to discolor under this treatment.

For small operations the double-boiler, so called, which is used for cooking cereals, is a handy and effective apparatus.

The National Formulary recommends that the salt be spread upon shallow trays or plates of glass and placed in an oven at 100°C . until it softens, usually 5 to 10 minutes, then taken out and immediately rubbed through a coarse tinned-iron sieve.

The hot method is used almost exclusively in manufacturing on the larger scale but it does not work with tartaric mixtures alone. Salts by this method must therefore contain either a considerable proportion of citric acid or of sugar. If large granules are desired tartaric acid is not ordinarily used.

The wet method is more convenient in most pharmacies, and gives just as good results when carefully performed.

It consists in moistening the mixed powders with a liquid which possesses only a slight solvent power upon it, and when the mass has become sticky drying it quickly by aid of a gentle heat.

Alcohol is most suitable for small quantities of salts.

The mixed powders are placed in a suitable dish, and alcohol gradually stirred in, until the mass coheres into small granular lumps. If large granules are not required no sifting is necessary, but when large granules are to be obtained the mass is made a little more moist, until relatively large lumps are formed, then these are broken up and the granules made even by sifting.

Do not use enough alcohol to make a paste, nor attempt to conform the granules to the size of sieve which is used. The granules are formed entirely by the cohesiveness of the moist mass, under the influence of kneading. In cold and dry weather the granulated salt is readily dried by spreading upon a tray or clean paper, which is then placed upon a register or radiator, or in any current of warm air.

In warm and muggy weather it is difficult to dry these salts thoroughly, and recourse must be had to a drying-oven or closet.

As soon as the salts are dry they may be sifted and the finer portions regranulated or saved for a future lot.

The granulated salt should then be bottled and the bottles tightly stoppered, as the salt soon loses its effervescing qualities on exposure of the air. They keep best when dried at a very low temperature, and if a drying-oven be used the heat should not exceed 100 to 110° F.

Manufacturers dry the granules in a vacuum dryer, which is the only safe method if the salts are to be stored for any time.

DIVIDING POWDERS

Guess-work is never proper in the dividing of powders.

When the powders are comparatively large and accurate dosage is not necessary, the powders may be divided by means of a cup-shaped measure.

These are often used in dividing seidlitz powders, but for such constant use they need to be standardized frequently. The edges of the cup wear away quickly, and the capacity of the cup gradually diminishes.

By far the best way for all kinds of powders, particularly if a large number of powders are to be made, is to weigh each separately. This can be done very quickly, as the hand and eye soon become accustomed to the necessary quantity, and after a few powders have been weighed approximately the right amount can be placed upon the balance each time, and the adjustment quickly made. Care must be taken, however, not to give overweight, particularly when a definite quantity of mixture is to be divided into a definite number of powders. It is very easy, for instance, in dividing 24 grains of mixture into 12 powders, to place $2\frac{1}{11}$ grains of powder upon the pan each time, and obtain 11 powders thereby, instead of 12, or by a slight deficiency in each weight to find a part of the mixture remaining after all the powders have been folded.

The Next Best.— It is much more difficult to weigh small powders satisfactorily than large ones, and for this reason most pharmacists prefer to divide these upon the pill-tile in a manner similar to the dividing of pills. The powder is placed upon the tile and built up into a rectangular pile, one edge of which is parallel and close to the division-scale of the tile. This is readily done by means of a couple of straight-edged spatules, care being taken to get the surface of the pile as well as the edges straight and even. The pile is now divided into the desired number of parts by cutting with the spatula, the division-scale serving as a guide.



FIG. 41.—Powder folders.

Occasionally a powder or a mixture is obtained which flows so easily that it cannot be built into a parallelogram; and this must be divided by weight, or by means of a suitable mechanical divider, of which there are several in the market.

PAPERS

The folding of powders in papers (*chartulæ*) is an art which is acquired only by practice.

When only two or three powders are dispensed at a time, they may be enclosed in a small envelope, but a number of powders are sent out preferably in a box. The papers should be selected to fit the powders, and folded to fit the box.

Hygroscopic, deliquescent, effervescent, or otherwise changeable substances, should be folded first in white calendered papers, then these are folded inside of paraffined or parchment papers to exclude moisture.

Powders intended for making lotions, or otherwise for external use, should be folded in colored papers as a distinguishing feature.

WAFERS

Wafers are folded by moistening one side of the wafer-paper before placing the powder upon it, then, while moist, folding in the same manner as a powder, but as small as possible. If too wet they do not fold nicely, and if not moistened enough they break, but a very little practice will enable one to get the proper degree of wetness, and they can then be folded as nicely and easily as papers. When dispensed the patient should be given explicit directions for taking them.

They are easily swallowed after soaking for a few seconds in a spoonful of water, and are tasteless. Do not soak long enough to cause them to break in the mouth.

CACHETS OR KONSEALS

In filling these care should be taken to get the whole of the powder in the center of the cachet. If any is spilled upon the edge the taste may be noticeable when the cachet is swallowed. In cachet-filling machines funnels are included for this purpose, as also some arrangement for moistening the edge of the cachet and pressing the two halves together. A little talcum on the plunger will prevent the powder or the cachet from sticking to it.

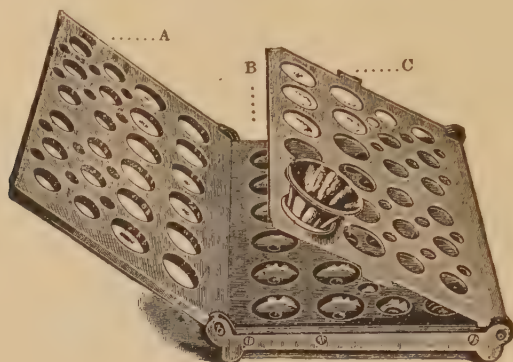


FIG. 42.—Cachet filler.

But little moistening is needed, just enough to cause the two parts to adhere. Too much moisture causes the edges to shrivel and the appearance is spoiled.

Like wafers, they are easily swallowed after dipping into water, and full directions for their administration should be given.

CAPSULES

Capsules are shells of gelatin into which medicinal bodies are put, and are designed to be swallowed in the same way as pills. The purpose of capsules is to cover the taste of the medicines, and any form of medication, dry, liquid or pasty, can be employed in capsule form.

There are two forms of capsules—hard capsules, *Capsulæ duræ* consisting of a deep cup-shaped form with a similar cover which closes the open end, and soft capsules, *Capsulæ molles* ovoid in form, of flexible gelatin, designed particularly for inclosing oils and non-aqueous liquid bodies, but often used for powders. Both kinds dry out and become brittle if stored in a dry and warm place. Their elasticity can be restored by placing them in a moist atmosphere—as in a box to the cover of which is fastened a wet sponge or cloth. Capsules are best stored in a moist and cool place.

Empty capsules in various sizes are purchased by the pharmacist, and it is the manner of filling them which concerns him particularly. Concerning the best method, there is a diversity of opinions, when the substance is in powder form.

Powders can be put into capsules in the powder form, or a pill-mass can be made and placed in the capsules. The latter is usually the easier method, and often makes the dispensing of a smaller capsule possible. But the massing of powders is not always permissible, and

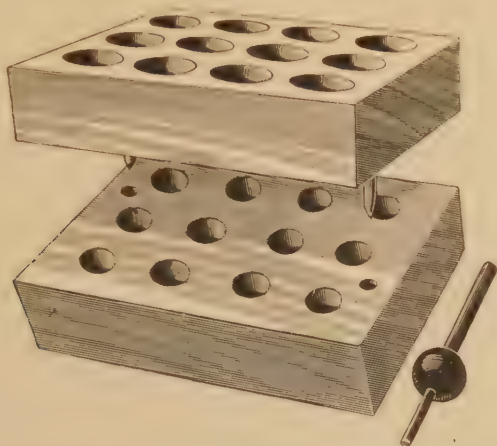


FIG. 43.—Capsule filler.

is frequently objected to by the physician, and then the capsules must be filled with the dry powder. When suitable funnels and holders are at hand the filling is an easy process, but without suitable apparatus it is a troublesome and particular operation to fill capsules

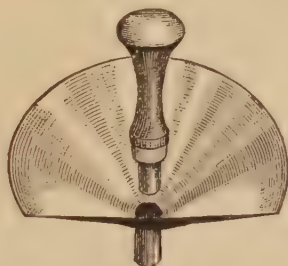


FIG. 44.—Capsule filler.

without leaving some on the outside to taste when the operation is finished. Since their chief purpose is to prevent taste, a slight trace on the outside may defeat this.

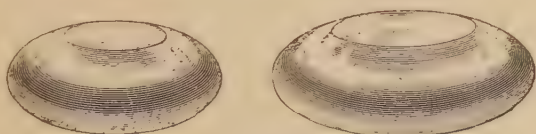


FIG. 45.—Gelatine globules.

There are several filling apparatuses in the market, all consisting of a holder for the main shell of the (hard) capsules, and a funnel

arrangement for pouring the powders into the capsule. A plunger of wood or metal serves to pack bulky powders into the capsule. When one of these apparatuses is used, the powders are mixed and divided in the usual manner, then instead of folding into papers, each powder is enclosed in a capsule. This method offers no special difficulties.

In the absence of a capsule-filling apparatus it is scarcely possible to avoid getting some of the powder on the outside of the capsule.



FIG. 46.—Soft gelatine capsules.

The usual method with mixed powders is to divide them as for papers, then taking the body of the capsules between the thumb and fingers of one hand and a spatula in the right, fill both cover and bottom by shoving through the powder repeatedly. The caps are then put on tightly, and the capsules are cleansed thoroughly with a cloth wetted with strong alcohol (if the powders are soluble in alcohol) or with diluted alcohol (if soluble in water) to remove that which adheres to the outside, then wiped dry. The cleaning should be thorough to prevent any taste of the powder when the capsules are filled, but water must not be used for this purpose.



FIG. 47.—Hard gelatine capsules.

When a single substance, in powder form, such as quinine sulphate, is to be put into capsules, it is the practice of some to omit the dividing and fill the capsules to the weight desired from a pile. The powder is poured upon a piece of clean paper, and the body of the capsule is plunged downward into it repeatedly until full. The cover may likewise be partially filled and the two when fitted together press the powder tightly inside. The capsules are then washed with alcohol, as above, and dried.

This method necessitates weighing each capsule as filled, with such repetitions in weighing each as may be necessary to secure accurate dosage. When a considerable number of capsules are to be filled, they can be done quite rapidly by this method.

Some powders lack adhesiveness and cannot be filled into capsules in this way, because they flow out when the capsules are lifted from the pile instead of adhering. These may be dampened with a little alcohol or water, as in making triturate tablets, and the damp powder will usually adhere. A mass should not be made. Or the powder may be pushed into the capsule with a spatula.

When a mass is made before inserting into capsules, the powders are massed as in making pills, and the mass rolled into a pipe and cut. The cut pieces should be as long as the closed capsule, and as large as will go into it. The hands are then washed, the piped pieces picked up with a pin and inserted into the capsule and the top put on. None of the substance is allowed to touch the outside of the capsule.

Mr. Alpers recommends that the mass be divided by weight instead of on a slab or pill machine.

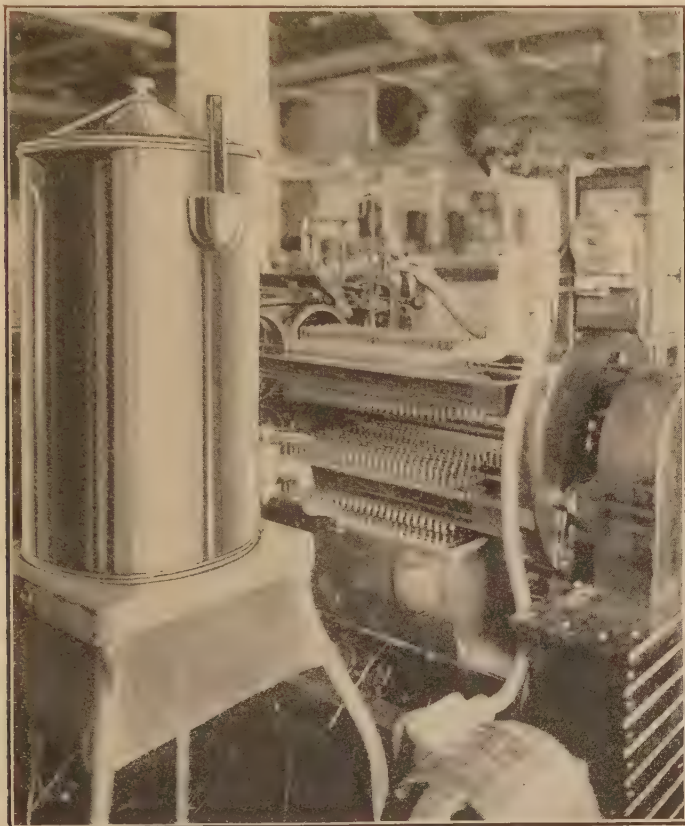


FIG. 48.—Capsule machine. Dipping.

Masses are allowable when the ingredients consist in part of liquid bodies which cannot be absorbed to form a powder without unduly increasing the bulk.

Also for aqueous fluids, which cannot be put into capsules in the fluid condition. Methylene-blue, a deep dyeing substance, is frequently ordered in capsules, and is such an intense coloring agent that it is a problem to avoid leaving the outside of the capsule colored. Some advocate making a mass of it, then rolling the pipes in charcoal and inserting. The charcoal prevents soiling the capsule when

inserted. Other powders may, if conditions require, be massed, but as a rule more satisfaction will be given the doctor and patient if powders are filled into capsules dry.

Liquids are usually dispensed in soft capsules, *i.e.*, capsules made of gelatin with enough glycerin to keep it flexible and slightly elastic. These are oviform and in one piece, with an elongated neck at one end.

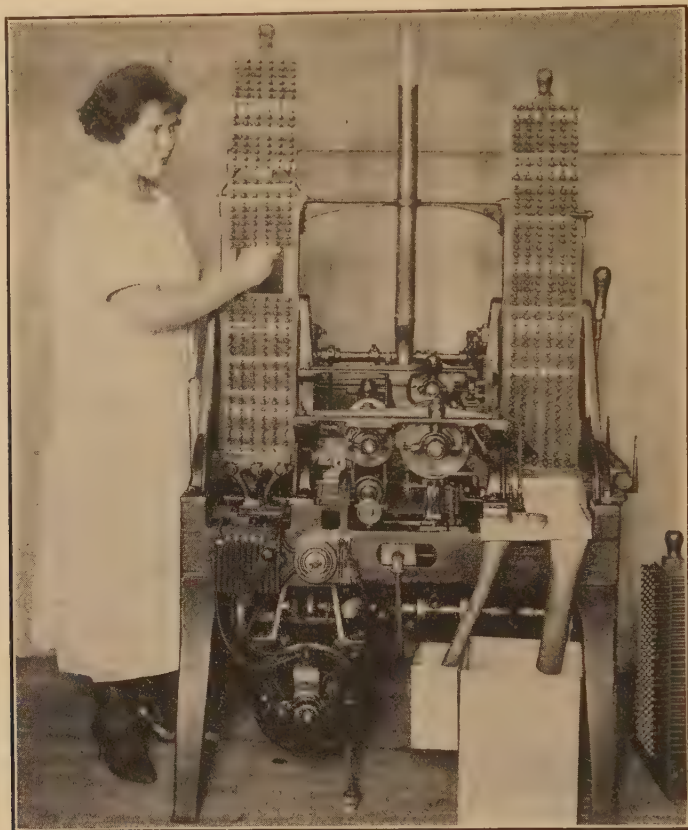


FIG. 49.—Capsule machine. Finishing.

When filled the necks are cut off, and the capsules are stood on end in sockets of wood or plaster of paris. The liquid is then dropped into them from a pipette, care being taken not to get any on the outside, then the capsules are sealed, either by melting the detached necks and applying the melted fluid to the open end of the capsule, or by pressing a hot spatula on the open end, which melts the gelatin and causes it to flow together. Traces of oil on the edge will prevent sealing of the capsule, by preventing adhesion. F. Apple recommends to wipe the necks of soft capsules with a bit of absorbent cotton moistened with chloroform, to remove traces of oil. After sealing the capsules should be set aside in a cool place for a few minutes to allow the gelatin-seal to set firmly.

Powders are occasionally, though rarely, put into these soft capsules. The powder should be poured in through a funnel to avoid getting any on the outside of the capsule.

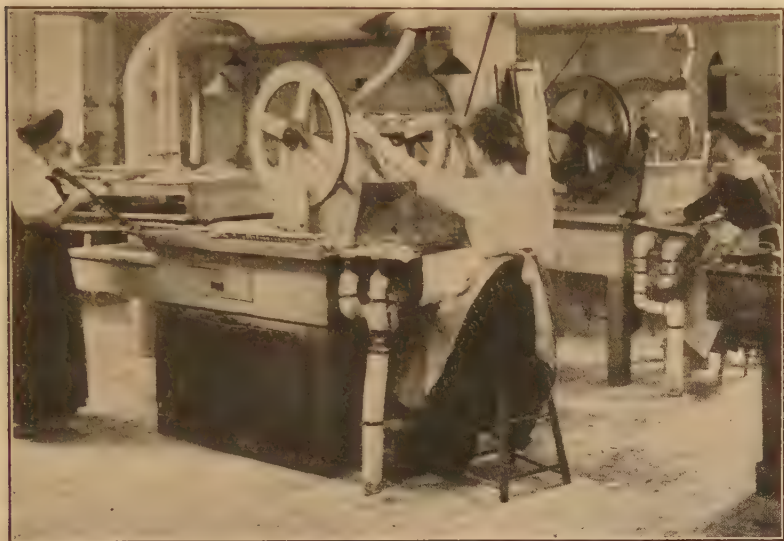


FIG. 50.—Making soft gelatine capsules or globules.



FIG. 51.—Filling and sealing soft capsules.

A powder-box cover set on an incline, or perforated to hold the capsules in position makes a good holder for the capsules while they are being filled.

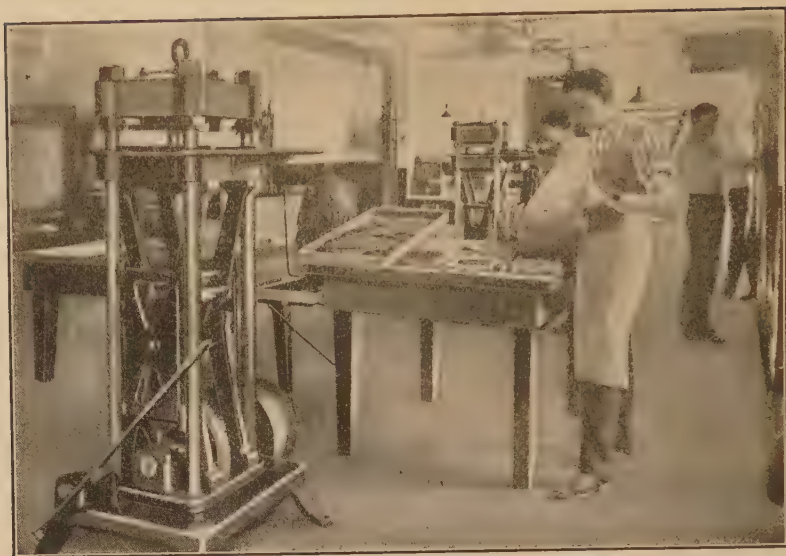


FIG. 52.—Press and apparatus for making gelatine pearls.

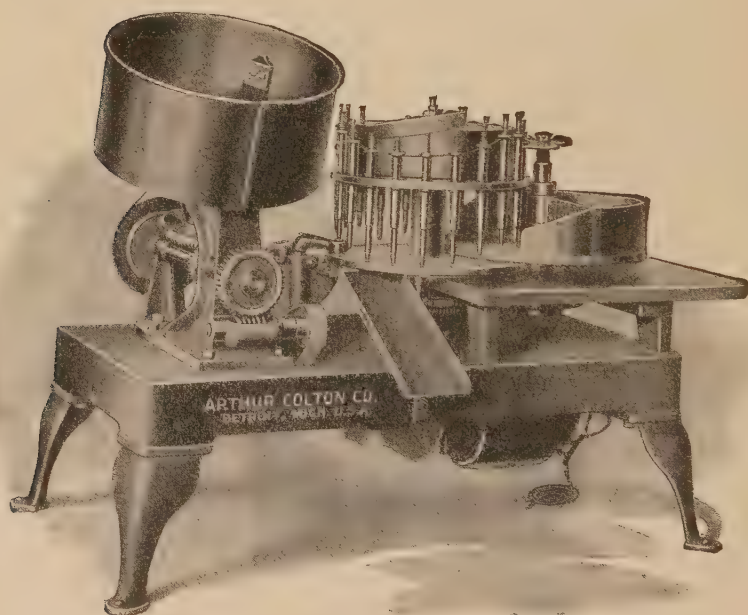


FIG. 53.—Automatic capsule filler.

Soft capsules should not be completely filled, but a small air-space left to preserve the elasticity. Aqueous fluids must not be put into capsules lest the gelatin be softened and the contents lost. Oils of all kinds are suitable for filling, also strong alcoholic fluids. Creosote, if put into *soft gelatin* capsules, must be first mixed with twice its volume of a bland oil or it will exude through the capsule. This is due to the solubility of creosote in glycerin, which perforates the capsule.

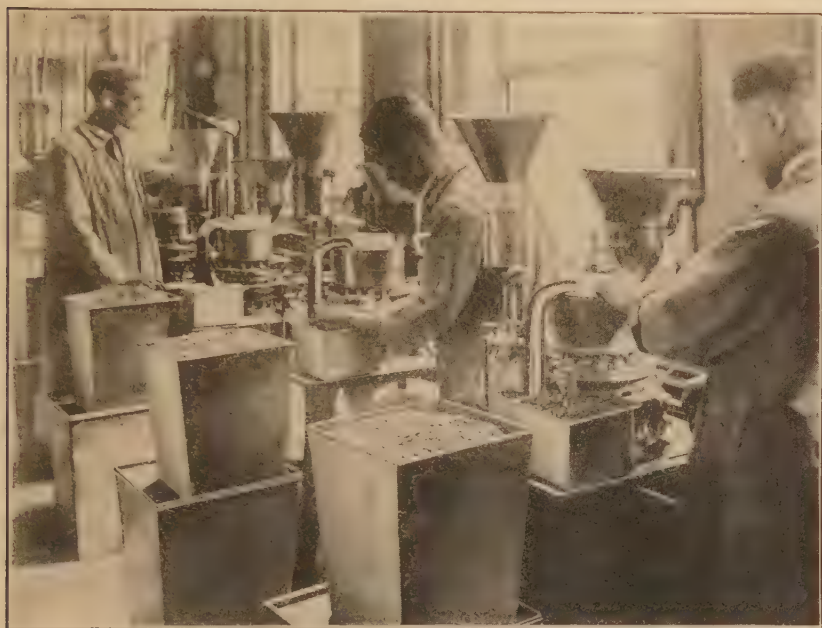


FIG. 54.—Capsule-filling machines.

Liquids may also be dispensed in hard capsules. In this case the liquid is dropped into the body of the capsule from a pipette, then the cap is moistened on the inner edge with water and pressed into place. The water softens the gelatin and seals the capsule. Creosote may be put into hard capsules without diluting, the capsules thus being smaller, but it is difficult to seal them so that they will not leak and is not often attempted.

W. G. Taplis has suggested the following method of putting volatile oils, terebene, etc., into hard capsules. The terebene or oil is first mixed with an equal weight of starch, and a very few drops of water is added to form a stiff mass, which is then piped and inserted as a mass. There is no danger of leaking in this method, wherein is an advantage.

Another form is known as pearls, and consists of spherical capsules completely filled with liquid or powder. These are beyond the domain of retail pharmacy, the capsules being made and filled at the same time. Special and expensive machinery is required, and the work cannot be done on a small scale. These often contain tablets as well as oils.

POWDERS

- 1
- R. Potassii chloratis.
Ammonii chloridi..... aa ij
Senegæ contusæ..... ʒ iv
Glycyrrhizæ contusæ..... ʒ ij
M. Ft. species.
Sig.—Make a quart of tea and drink
half a wine-glassful every hour.
- 3
- R. Althææ..... 8
Verbasci foliæ..... 2
Glycyrrhizæ..... 3
Tussilaginis..... 4
Anisi..... 2
Iridis..... 1
Contundantur et miscentur.
Sig.—“Breast Tea, N. F.”
- 5
- Ceylon cinnamon, in fine
powder..... 35 Gm.
Ginger, in fine powder... 35 Gm.
Cardamom, deprived of
the capsules and crushed 15 Gm.
Nutmeg, freshly grated.. 15 Gm.
Sig.—Aromatic powder, N. F.
- 6
- R. Sulphuris præcip..... 7.5
Guaiaci..... 5.0
Magnesiæ..... 10.0
M. Sig.—Teaspoonful twice a day.
- 7
- R. Pulv. rhei..... 35
Magnesiæ pond..... 65
Anetholis..... 8
Alcoholis..... 10
M. Sig.—Compound anise powder.
- 9
- R. Acidi salicylici..... 0.3
Acidi borici..... 1.0
Pulveris talci..... 8.7
M. Ft. pulv. subtilis. Sig.—“Salicy-
lated talcum powder, N. F.”
- 11
- R. Amyli..... 16.0
Zinci oxidi..... 8.0
Camphoræ..... 1.0
M. Ft. pulv. subtil. Sig.—“Dust-
ing powder.”
- 2
- R. Sennæ..... 16
Sambuci florum..... aa 10
Fœniculi..... 5
Anisi..... 5
Potassii bitartratis..... 4
Contusa et misce.
Sig.—Laxative species, N. F.
(St. Germain Tea.)
- 4
- Prepared chalk..... 30 Gm.
Acacia, in fine powder... 20 Gm.
Sugar, in fine powder.... 50 Gm.
“Mix them intimately.”
Sig.—Compound chalk powder.
Make one-tenth the quantity.
- 5
- “Triturate the cardamom and nut-
meg with a portion of the Ceylon cinna-
mon, until they are reduced to a fine
powder; then add the remainder of the
cinnamon and the ginger, and rub them
together until they are thoroughly
mixed.”
Make 10 grams.
- 6
- Triturate the magnesia and guaiac
together, then mix these with the sul-
phur by trituration.
The mixture should readily diffuse
through water.
- 8
- R. Naphthalini..... 10.00
Acid borici..... 10.00
Camphoræ..... 0.40
M. Ft. pulv. subtilis. Sig.—Use as
a snuff.
- 10
- R. Zinci oxidi..... ʒ iv
Acidi carbolici..... gr. viij
Acidi tannici..... ʒ ss
Amyli..... ʒ iij
M. Sig.—Dusting powder.
- 12
- R. Saccharini,
Mentholis
Thymolis..... aa 1
Olei cinnamomi..... 2
Saponis pulv..... 50
Cretæ præcip..... ad 1000
M. Sig.—Tooth powder.

13

- R. Pulv. amygdal. amaræ sine
cortice et oleo 3 vj
Farinæ tritici,
Pulv. iridis.....aa 3 iv
Saponis pulveris,
Sodii boratis.....aa 3 j
Olei amygdal. amaræ..... gtt. x
Olei bergamottæ..... 3 ij
Tinct. moschi..... 5 j
M. Sig.—Almond meal.

14

- R. Ipecac, in fine powder.... 10 Gm.
Powdered opium..... 10 Gm.
Sugar of milk in moder-
ately coarse powder..... 80 Gm.
M. Sig.—Dover's powder.
- "Rub them together into a very fine powder."
Make one-tenth of the quantity.

15

- R. Pulveris Doveri.....5 j
In pulveres vi. divide et mitte
in capsulæ amylaceæ.
Sig.—10-grain Dover's powder.

16

- Morphine sulphate..... 1 Gm.
Camphor..... 19 Gm.
Glycyrrhiza, in fine powder 20 Gm.
Precipitated calcium car-
bonate..... 20 Gm.
Alcohol, a sufficient quan-
tity.
M. Sig.—Tully's powder.
- "Rub the camphor with a little alcohol, and afterward with the glycyrrhiza and precipitated calcium carbonate, until a uniform powder is produced. Then rub the morphine sulphate with this powder, gradually added, until the whole is thoroughly mixed. Finally pass the powder through a No. 40 sieve, and transfer it to well-stoppered bottles."
Make one-sixth the quantity.

17

- R. Pulv. morphinæ comp..... 5 j
In pulveres vi. divide et mitte
in chartulæ amylaceæ.
Sig.—10-gr. Tully's powders.

18

- R. Aquilæ albæ..... gr. iss
Sacchari lactis..... 5 j
M. Ft. chartulæ xij no.
Sig.—Calomel triturates.
(Aquila alba—old name for calomel.)
- Triturate very thoroughly together.

19

- R. Sodii salicylatis..... 1.30
Sodii bicarbonatis..... 2.00
M. In pulveres decem divide.
Sig.—Capiat pulverem unam ex
aqua gelida cyathis post cibo

20

- R. Calomelatis..... gr. x
Magisterii bismuthi..... gr. xx
Salaerati..... gr. xl
M. Sig.—Ut dictum.
- Triturate the calomel thoroughly with the powdered potassium bicarbonate, then add the bismuth subnitrate and mix gently.

21

- R. Bismuthi salicylat.,
 Salol.....āā 10.00
 M. Ft. chart. xxiv no.

These make a slippery powder, which cannot be divided accurately in the usual manner. Each powder should be weighed.

22

- R. Pulveris thebaicæ..... 0.325
 Magisterii bismuthi..... 3.250
 Misce in chartulas decem dividenda.
 Sig.—Opium and bismuth

23

- R. Pepsinæ..... 2.0
 Bismuthi subnitrat..... 5.0
 Magnesii carbonat..... 3.0
 Pulv. aromatici..... 1.0
 M. et in chart. xij divide.
 Sig.—Capiat unam post cibo.

Mix on paper. Do not triturate.

24

- R. Hydrarg. submur..... gr. ij
 Pulv. rad. rhei..... gr. v
 Elæo acch. menth. pip... 3 ss
 M. Ft. pulv. dent. tal. dos. xi no.
 Dent. in chart. cerat. Sig.—Hora
 decubitus sumatur unum.

25

- R. Sodii boratis,
 Acidi borici,
 Aluminis.....āā 15.0
 Acid carbolic,
 Ol cassiæ..... āā 1.0
 M. Sig.—A teaspoonful in a pint of
 warm water.

26

- R. Tinct. opii..... 1.0
 Plumbi acetatis..... 1.0
 Sacchari..... 2.0
 M. Ft. pulv. vi no. Sig.—P. r. n.

Triturate the tincture with the sugar, dry in a warm (not very hot) place, and add the sugar of lead, mixing thoroughly.

27

- R. Phenacetin..... gr. v
 Caffeinæ citrat..... gr. ss
 M. Ft. pulv. et mitte tales vi no.
 Sig.—Sumat nocte.

28

- R. Phenacetin,
 Salol.....āā gr. v
 Caffeinæ citrat..... gr. ss
 Hydrarg. chlor. mit..... gr. 1/10
 M. Ft. pulv. j no. Disp. pulv. tales
 no. xij.
 Sig.—Ut. dict.

29

- R. Potassii chlorat..... 3 ij
 Acidi tannici..... 5 i
 Sacchari..... 3 ij
 M. Ft. chart. xij no. Sig.—One in
 a tumblerful of cold water, for a
 gargle.

Powder the ingredients separately, and mix very lightly on paper.

30

- R. Ammon. carbonat..... 5 ss
 Pulv. Tullii..... 5 j
 M. et in pulv. vi no. divid. Sig.—
 One at night.

Mix quickly and dispense in double papers, the outer paper being waxed.

31

- R. Ammon. bromidi..... 3 ss
 Sodii bicarbonat..... 3 ss
 M. et in chart. xij divide. Detur in
 scatula.

If the salts are not perfectly dry, ammonia gas will be liberated.
 Mix lightly and fold in paraffin papers.

32

- R. Quininae sulphatis..... gr. ij
 Ammonii carbonatis..... gr. iv
 Misce et detur tales numero
 quatuor in chartæ ceratæ.
 Sig.—Sumatur una nocte manequæ.

34

- R. Elaterini..... gr. ii
 Capsici..... gr. ij
 Ol. tigllii..... m. vj
 M. et in partes æquales xij divide.
 Dentur in capsulæ.

35

- R. Salolis..... gr. xlv
 Thymolis..... gr. xxx
 Bismuthi subnit..... gr. lxxv
 M. Ft. kons. xv no.

36

- R. Antipyrini..... gr. iv
 Caffeinae citrat..... gr. i
 Sodii bromid..... gr. viiiss
 M. Ft. chart. tales xx no.

37

- R. Acidi salicylici..... gr. x
 Phenolis..... gr. ii
 Eucalyptolis..... m. ii
 Mentholis..... gr. ii
 Thymolis..... gr. ii
 Zinci sulphatis..... 5 iv
 Acidi borici..... ad. 3 iv
 M. s. a. Sig.—Antiseptic powder.

38

- R. Asafœtidæ,
 Creosoti,
 Phenyl salicylat..... ãã gr. ii
 M. Ft. capsul i no. mitte xii.

39

- R. Bismuthi betanaphthol..... 6.5
 Creosoti..... 0.6
 Zingiberis pulv..... 2.0
 M. Ft. capsul xxx no.
 Sig.—One as directed.

40

- R. Ichthyoli..... m. x.
 Mitte in capsulas tales no. xii.
 Sig.—One three times a day.

41

- R. Magnesii sulphatis exsic..... 3
 Sodii sulphatis exsic..... 3
 Potassii bicarbonatis..... 10.5
 Sodii bicarbonatis..... 9.5
 Acidi tartarici..... 14.0
 Sacchari pulv..... 11.0
 M. Ft. pulv. effervesc. Da in
 ampulla.

17

33

- R. Olei ricini..... 50.0
 Magnesiae..... 50.0
 M. Ft. pulv. Sig.—Castor Oil
 powder. Two tablespoonfuls in
 water.

Make a soft mass by means of a little
 powdered soap and water.

Makes a pasty mass. Dunning mixed
 the salol and bismuth, divided into
 konseals, and added a 2 gr. capsule of
 thymol to each, before sealing.

Becomes pasty. Use 1/2 gr. caffeine
 in place of the citrated caffeine and
 add sufficient magnesia to absorb the
 moisture.

Mix the first five ingredients and mix
 the resulting liquid with the zinc sul-
 phate and boric acid.

Dissolve the salol in the creosote, add
 the asafœtida and enough flour to
 make a mass.

Care is needed to distribute the creosote
 evenly. Mix first with the ginger,
 then with the bismuth.

Ammonium ichthyolate will soften
 the capsules and give trouble. Use
 sodium ichthyolate and dispense in hard
 capsules.

(About 18 Gm. of Rochelle salt are
 formed when this is dissolved.)

42

- R. Potass. bromidi..... 16.6
 Sodii bicarbonatis..... 53.0
 Acidi citrici..... 25.0
 Acidi tartarici..... 20.4
 M. Ft. pulv. efferv. s. a.
 Sig.—Effervescent potassium
 bromid:

43

- R. Sodii phosph. exsic.... 24.00 Gm.
 Sodii bicarbonatis..... 57.25 Gm.
 Acidi tartarici..... 30.25 Gm.
 Acidi citrici..... 19.42 Gm.
 M. Ft. pulv. effervesc. s. a.
 Sig.—Effervescent sodium phos-
 phate.

44

- R. Sodii bicarbonat..... 14.5
 Potassii bicarbonat..... 8.0
 Acidi citrici..... 9.0
 Acidi tartarici..... 12.0
 Sacchari pulv..... 6.5
 M. Ft. pulv. effervesc. s. a. Da in
 ampulla.

When this mixture is dissolved in water 22.5 parts of Rochelle salt are formed by the reaction between the bicarbonate and tartaric acid. Sodium citrate is also formed.

45

Sodii Sulphas Effervescens [Ph. Br.].

- R. Sodium sulphate..... 100 Gm.
 Sodium bicarbonate..... 100 Gm.
 Tartaric acid..... 54 Gm.
 Citric acid..... 36 Gm.

Dry the sodium sulphate until it has lost 56 per cent of its weight, powder the product and mix it with the other ingredients.

Granulate in the same manner as Magnesii Sulphas Effervescens.

46

Magnesii Sulphas Effervescens [Ph. Br.].

- R. Magnesium sulphate... 50 Gm.
 Sodium bicarbonate... 36 Gm.
 Tartaric acid..... 19 Gm.
 Citric acid..... 12.5 Gm.
 Powdered sugar..... 10.5 Gm.

Dry the magnesium sulphate at about 54° C. (130° F.) until it has lost 23 per cent of its weight, powder the product and mix it with the sugar, then with the other ingredients. Place the mixture in a suitable dish heated to between 200° and 220° F., and when the particles of powder begin to aggregate, stir assiduously until they assume a granular form; then separate the granules into uniform sizes by sifting and preserve the product in well-stoppered bottles.

47

- R. Sodii bromidi..... 4.0
 Validol..... 4.0
 Magnesiae calc..... 0.8
 M. Ft. capsul xii no.

The calcined magnesia prevents a pasty mass if doubled in quantity, absorbing the moisture. (Lascoff.)

48

- R. Tinct. opii. deod..... 3 ss
 Tinct. hyoscyami..... 3 ss
 Olei santali..... 3 ss
 Copaibæ..... gr. xx
 M. Ft. capsul xii no.

Evaporate the tinctures to a soft extract at a low heat. Mass the oil and copaiba with a little magnesia and incorporate the extracts, then roll into a pipe and divide.

49

- R. Urotropin..... gr. xv
 Calcidin..... gr. xv
 Aspirin..... 5 i
 M. Ft. capsul. xx no.
 Sig.—As directed.

The urotropin (hexamethylenamine) and aspirin (acetylsalicylic acid) form a liquid when mixed.

50

- R. Phenacetin..... gr. i
 Aspirin..... gr. ii
 Euquinine..... gr. ii
 M. Ft. caps. No. 1. Disp. tales no. xii.
 Aspirin and euquinine liquefy when mixed. The addition of 3 grains of dried starch to each capsule prevented this change. (Linton).

Prescriptions from State Board Examinations

FOR CRITICISM AND PRACTICE

I

- R. Hydrarg. chlor. mit.,
 Sodæ bicarb.....āā ʒi
 M. Ft. pulv. vi. no. Sig.—One at night. (Wash.)

3

- R. Antipyrini..... gr. xx
 Hydrarg. subchlor..... ʒ ss
 Sacchari pulv..... ʒ i
 Misc. Ft. pulv. x no.
 Sig.—One as directed. (N. Y.)

5

- R. Potassii chlorat..... ʒ ii
 Acidi tannici..... gr. iv
 Olei menth. pip..... m ii
 M. Ft. pulvis. (Ill.)

7

- R. Pulv. rhei..... gr. xxiv
 Magnesii carb..... gr. xviii
 Ol menth. pip..... gtt vi
 Alcoholis..... gtt xii
 Tere simul et in chartulas no. vi divide. Sig.—One p. r. n. (Ill.)

9

- R. Camphoræ..... gr. xxx
 Chloral hydrat..... gr. xxx
 Sacchari alb..... gr. xx
 M. Ft. chart x no. (Neb.)

11

- R. Phenyl salicylat..... gr. ii
 Ol. santali,
 Ol. cubebæ,
 Ol gaulther.....āā m. i
 Fac. capsulum unum.
 Mitte tales dosas vi no.
 Sig.—Two as directed. (Tex.)

13

- R. Codeinæ sulph..... ʒ iss
 Terpin hydrat..... ʒ iii
 Pulv. ipecac..... ʒ i
 M. et in caps. xl. divide.
 Sig.—One every 3 hours. (Minn.)

2

- R. Morphinae sulph..... gr. i
 Camphoræ..... gr. x
 Sacchari..... ʒ i
 M. Ft. pulv. d. t. d. vi no.
 Sig.—One every 2 hours. (N. Y.)

4

- R. Sodii salicylatis..... gr. xx
 Caffeinæ..... gr. iv
 Acetanilidi..... gr. iii
 Camphoræ..... gr. xx
 Fiant chartulæ vi no.
 Sig.—One every 3 hours, as directed. (Tex.)

6

- R. Bismuthi salicylat,
 Salol.....āā 4.00
 M. Ft. chart xii no.
 Sig.—One powder every 3 or 4 hours. (Ill.)

8

- R. Potass. chlorat..... gr. xxx
 Ext. belladon..... gr. iiss
 Tritici..... ʒ iv
 M. Ft. chart. i no. Mitte x no.
 Sig.—One in a pint of water as directed. (Neb.)

10

- R. Santonini..... gr. xii
 Hyd. chlor. mit..... gr. vi
 Sacch. lactis..... gr. xx
 Fiant chart. vi no.
 Sig.—One as directed. For little Mary Harris. (Tex.)

12

- R. Terpini hydrat..... gr. vii
 Duotal..... gr. xii
 Codeinæ..... gr. i
 Strych. sulph..... gr. 1/16
 Misce et pone in caps vi no.
 Sig.—One or two qq. 4 hours. (Tex.)

14

- R. Creosoti..... m. xx
 Eucalyptol..... m. xl
 M. Ft. caps. xx no.
 Sig.—One 3 times a day. (Mo.)

15

- R. Sodii salicylat,
Pulv. aloes.....āā gr. iii
M. Ft. caps. tales vi no.
Sig.—One h. s. (Ill.)

17

- R. Salol..... 3 i
Betanaphthol..... gr. xxiv
Acetamididi..... gr. xxxvi
Caffeinæ cit..... gr. xviii
M. et div. in capsul xii no.
Sig.—One capsule every 2 hours.
(Pa.)

19

- R. Ext. belladon. pulv..... 3 iss
Sodii salicylat..... 3 ii
M. et in caps. xxiv div.
Sig.—One every 4 hours. (Mont.)

21

- R. Ext. nucis. vomic..... 3 i
Sodii bicarb..... 3 iii
M. et in capsul. v. no. divide.
Sig.—One before meals. (S. D.)

23

- R. Creosoti..... m. xx
Eucalyptol..... m. xl
M. Ft. capsul. xx no.
Sig.—One three times a day.
(Mass.)

25

- R. Strych. sulph..... 0.016
Salolis..... 0.775
Salicini..... 1.296
Quininæ sulph..... 1.944
M. Ft. caps. xii no.
Sig.—One t. i. d. (Tex.)

27

- R. Quininæ sulph..... gr. iss
Antifebrin..... gr. iii
M. Ft. pulv. mitte vi.
Sig.—Cap. unum si opus sit.
(Br. Col.)

29

- R. Pulv. rhei..... gr. xxiv
Magnesii carb..... gr. xviii
Ol. menth. pip..... gtt vi
Alcoholis..... gtt xii
Tere simul et in chartulas vi no.
divide.
Sig.—One p. r. n.

31

- R. Morphinæ sulph..... gr. x
Pulv. ipecac..... 9 ss
Pulv. sacchari..... 3 i
M. et in pulv x. divide. (N. Y.)

16

- R. Resorcinolis..... gr. vi
Salol..... gr. vi
Bismuthi subgallat..... gr. xii
M. et ft. capsul vi no. (Mass.)

18

- R. Aspirin,
Ammon. carb.,
Sod. salicylat.....āā gr. xxx
M. Ft. caps. xii no.
Sig.—One every 4 hours. (N. C.)

20

- R. Acidi arsenosi..... gr. iss
Pil. ferri. carb..... 3 iiss
M. et in capsul xxx no. div.
Sig.—One after meals. (S. D.)

22

- R. Phenylis salicylat.,
Olei. ricini.....āā 0.3
M. Ft. caps. d. t. d. iii no. (N. Y.)

24

- R. Hydrarg. chlor. mit..... gr. i
Cinchonid. salicylat..... gr. xx
M. Ft. capsul. vi no.
Sig.—One every 3 hours. (Ill.)

26

- R. Antipyrini..... 3 i
Sodii salicylat..... 3 i
M. Ft. capsul. xii no.
Sig.—One every 4 hours.

28

- R. Bismuthi salicylat.,
Salol.....āā 4.00
M. Ft. chart. xii no.
Sig.—One powder every 3 or 4
hours. (Ill.)

30

- R. Aluminis..... 3 iv
Sodii boratis..... 3 vi
M. (N. Y.)

32

- R. Salol..... gr. xx
Camphoræ..... gr. x
Pulv. ipecac et opii..... gr. x
M. Ft. chart. x no.
Sig. Take a powder every 3 hours.
(New Mex.)

33

- R. Pepsini ℥ i
 Pulv. zingib. ℥ ss
 Magnes. carb. ℥ ii
 M. et in pulv. xii no. div.
 Sig.—Cap. unum semih. p. c. si op.
 sit. (Br. Col.)

35

- R. Morphinae sulph. gr. xvi
 Quininae sulph. gr. i
 Pulv. capsici. gr. iii
 M. Ft. chart viii no.
 Sig.—One powder every 3 hours.
 (N. Y.)

37

- R. Acid acetylsalic. 4.0
 Pulv. camphoræ. 1.0
 Pulv. ipecac. 0.9
 Pulv. opii. 0.9
 M. et ft. caps no. xii.
 Sig.—One q. 4 h. (Fla.)

39

- R. Arseni trioxid
 Strychninae sulph. āā 0.033
 Ferri reducti. 0.650
 M. et in caps x no divid.
 Sig.—Caps. t. i. d. p. c. (Col.)

41

- R. Hydrarg. chl. mit. gr. xx
 Bis. subgallat. gr. xx
 M. Ft. chart no. xx.
 Sig.—One every 4 hours. (Tex.)

43

- R. Gray powder. 0.65
 Pulv. rhei. 0.065
 Pulv. ipecac. 0.15
 Sodii bicarb. 0.30
 M. D. i. d. pulv no. x.
 Sig.—One a. c. t. i. d. (N. C.)

34

- R. Sodii salicylat. gr. xx
 Caffeinae. gr. iv
 Acetanilidi. gr. iii
 Camphoræ. gr. xx
 M. Ft. chart. vi no.
 Sig.—One every 3 hours as directed.
 (Iowa.)

36

- R. Aspirin. ℥ i
 Quinine sulph. ℥ i
 M. Ft. cap. no. xii.
 Sig.—One every 3 hours. (Tex.)

38

- R. Aspirin. 4.0
 Salol. 3.0
 Pulv ipecac et opii. 2.0
 Camphoræ. 1.0
 Atropinae sulph. 0.1
 M. Ft. chart xii no.
 Sig.—One q. 3 hr. (Fla.)

40

- R. Hydrarg. protojodid. gr. i
 Pulv. mimosæ
 Sacchari alb. āā gr. x
 M. Ft. pulvis subtil; divid. in cht. decem.
 Sig.—One powder twice daily.
 (Mo.)

42

- R. Methenaminae 0.4
 Potass. acetatis. 0.8
 M. Ft. caps. no. xii.
 Sig.—One every 3 hours. (N. C.)

44

- R. Bismuth subgallat. ℥ i
 Camphoræ. ℥ ss
 M. Ft. pulv xii no. (N. C.)

CHAPTER XII

SUPPOSITORIES, BOUGIES, PESSARIES, POLITZER PLUGS

Suppository (Lat. *Suppositorium-i*).—A solid medicated substance, usually of a conical form, designed for introduction into the passages of the body, there to be absorbed.

Bougie (Lat. *Bougia-æ* or *Bacillum-i*).—This term *bougie* (bōō-zhe) is properly employed to designate solid and insoluble or non-absorbable bodies intended to be introduced into passages for the purpose of dilation. These are composed of silver, steel, wax, rubber, gum, etc., and are sometimes smeared with medicinal substances when a medicinal as well as a mechanical action is desired.

The term is often used to designate medicated suppositories of gelatin, wax, cacao butter and wax, etc., for nasal or urethral use.

Pessaries (Lat. *Pessum-i* or *Pessarium-i*).—In like manner the term *pessary* properly denotes an instrument introduced into the vagina for the support of the uterus, but is often applied to vaginal suppositories.

Politzer Plugs.—Plugs of greased cotton for insertion into the ear. Used for protection after operations on the ear.

This form of medication may be intended for local diseases or for general absorption. Medicines introduced into the rectum in a proper condition will produce their characteristic effects upon the system in the same way as when swallowed. Foods are also given in this manner in special cases, as after surgical operations, or when the stomach is in an irritable or weak condition and is unfitted for the reception of food or medicines. Suppositories are generally employed for local treatment, as in hemorrhoids, or when for any reason, medicines cannot be taken into the stomach. As a rule, medicines act more slowly in this form and slightly larger doses are required than when administered by the mouth.

Strychnine is, however, a notable exception.

ESSENTIALS

Suppositories should be of firm consistence when cold, should melt at or slightly below the temperature of the body (98° F.), should be non-irritating, and must not become rancid.

The size and shape are governed by the use to which the suppository is to be put. Those designed for the rectum or vagina are usually bullet or cone-shaped, the vaginal suppositories being made about twice as large as the rectal.

Suppositories designed for the urethra or nasal passages are made into slender rolls $\frac{3}{4}$ inch to 2 inches in length, pointed at one end and weighing from 10 to 30 grains. Urethral suppositories made of gelatin are sometimes directed as long as 6 inches.

Suppositories for the aural cavities are a compromise between the two forms, or are cartridge-shaped and weigh 5 to 10 grains.

Suppositories were first introduced into the U. S. Pharmacopœia in 1870.

The present Pharmacopœia requires that rectal suppositories shall be cone-shaped, and if of cacao butter shall weigh about 2 Gm., or 4 Gm. if of glycerinated gelatin; urethral suppositories pencil-shaped, and shall contain 2 to 4 Gm. of glycono-gelatin vehicle, or about 1 to 2 Gm. of cacao butter; and vaginal suppositories globular and weigh about 4 Gm., if of cacao butter, or 10 Gm. if of glycono-gelatin.

BASES

Cacao butter¹ (*Oleum Theobromatis*) is probably the best general base for suppositories, and should be used for prescriptions unless another base is designated.

This is hard and wax-like at ordinary temperatures, but melts at 86° to 94° F., has a specific gravity of about 0.973, and can be readily incorporated with small portions of aqueous substances, or with oils, etc., and does not readily become rancid.

When mixed with volatile oils, chloral, creosote, phenol, etc., the melting-point is lowered to a considerable extent. This may be corrected by adding spermaceti. Castor oil also has a peculiar stiffening effect, and is preferable to wax, particularly for chloral suppositories. If needed, equal parts of spermaceti and cacao butter may be used. A mixture of 7 parts of cacao butter with 1 of spermaceti has been recommended for suppositories and bougies which are desired to melt very slowly, and thus exert a prolonged action.

Spermaceti is sometimes added to those which are designed to absorb very slowly, as in hemorrhoids, etc., in order to bring the melting-point of the suppository to as near the temperature of the body as possible. A mixture of 7 parts of cacao butter and 1 part of spermaceti melts near to 98° F.

Wax gradually hardens on standing and is not as safe as spermaceti for raising the melting-point.

Freshly melted cacao butter shows a considerably **lower melting point** than the normal one, and only regains the normal melting point after standing for a number of days in a cool place. This means that when suppositories are made with cacao butter by the hot process the freshly made suppositories will be softer and will melt more readily than after they have stood five or six days and longer. When spermaceti or wax is added to make a firmer suppository care must be taken that too much wax is not added. The suppositories may melt readily at body temperature when first made, but may harden to such an extent as to become useless as a remedy after standing a few days. Ordinarily more than 5 per cent of wax or 10 per cent of spermaceti should be regarded as suspicious. But large amounts of fat-soluble substances may justify more. One writer states that cacao butter, after melting, does not return to its original condition until it has stood twenty-six days. In other words the melting point remains below normal for twenty-six days after the melting.

¹ Cacao butter or cocoa butter (the first term is preferable) is a concrete oil obtained from the seeds of *theobroma cacao*, or chocolate plant. It is separated from chocolate by heavy pressure between heated plates, and commercially is a by-product of the manufacture of cocoa for drinking or flavoring purposes. It should not be confounded with coconut butter, a semi-solid oil obtained from coconuts (*cocos nucifera*) which is not firm enough to use for making suppositories.

Lard should not be used in suppositories, because of its tendency to become rancid.

Dunning recommends a mixture of 82.5 parts of cacao butter, 12 parts of castor oil and 2.5 parts of white wax for use in summer.

Lanolin is a useful adjunct to suppositories containing large amounts of extracts or aqueous fluids. This absorbs the liquid better than cacao butter, mixes well with the latter, and affects the fusing point but little. Lanolin is also more readily absorbed.

Hollow suppositories of cacao butter were introduced into pharmacy some years ago.

These come in the various forms and sizes and resemble the ordinary moulded suppository, but consist only of a thick shell of cacao butter, with an opening at the top for the introduction of the medicinal matter. A cap or plug of cacao butter, which is slightly warmed just before inserting to soften its surface, serves to seal the suppository after the

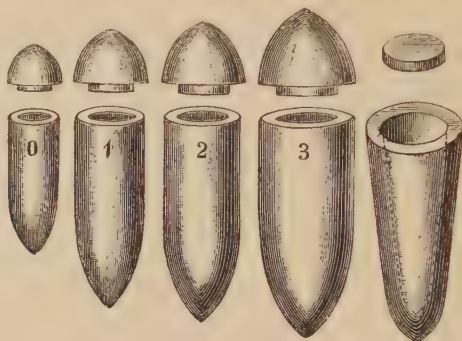


FIG. 55.—Hollow suppositories of cacao butter.

medicaments have been placed inside. These are intended to be used in place of the usual forms, but have not proved acceptable for several reasons. The labor of mixing, dividing, and inserting the medicinal matter, particularly when extracts are used, is often as great as that involved in making a corresponding suppository entire, either by hot or cold process; no medicinal effect can be produced until the suppository has entirely melted, and then the condition of the medicament may not be the best for absorption; and the appearance of the suppository offers no clue to the nature, condition, or strength of its contents.

Soap is sometimes used as a base for suppositories, particularly when a laxative action is desired. Soap cones, made from ordinary castile soap, are used to produce evacuation of the bowels, which it causes by a slight irritant action.

The British Pharmacopœia uses a mixture of curd-soap (a soap made with soda and a purified animal fat) and glycerite of starch, stiffened, if necessary, with a little powdered starch, for its phenol suppositories, morphine suppositories with soap, and tannic acid suppositories with soap.

These are made by the cold process, shaping the suppositories by hand.

The glycerin suppositories of the U. S. Pharmacopœia have a similar soap base, but without the starch.

It should be remembered that, in making suppositories with a soap base, **soap is incompatible with metallic salts**, forming an insoluble metallic soap, and hence is unsuitable for such. Soap also affords a good medium for incorporating aqueous fluids with cacao butter.

Gelatin is preferred for bougies and soluble pessaries, and at times for vaginal or glycerin suppositories.

Gelatin is soluble in hot water and in hot glycerin, the solutions becoming firm and elastic when cold if more than 5 per cent of gelatin is present. Salts and acids tend to liquefy gelatin, thus softening the suppository, while tannin, alum, creosote, formalin, etc., form an insoluble compound and thus make a hard and less soluble suppository. Gelatin suppositories containing glycerin, and no water, change less readily than a hydrated gelatin base. Professor Hallberg recommended the following **Anhydrous Glycero-gelatin** for general use, which has since been adopted by the Pharmacopœia. One hundred grams of gelatin are covered with cold sterile water, allowed to stand one hour, then the water is drained off. One hundred grams of glycerin is then added, and the whole is heated on a water-bath in a tared dish until the gelatin is liquefied and the whole product weighs 200 grams. The liquid is strained and allowed to solidify. When medicated suppositories are made with this, the substance, if very soluble in water, is dissolved in a little water, enough glycerin is added to weigh one-half the total quantity required, and an equal weight of the glycero-gelatin is then melted, the solution is added, and the mixture poured at once into moulds. The moulds may be lightly greased with petrolatum.

Insoluble powders—as iodoform, carbonates, oxides, etc.—should be thoroughly rubbed with glycerin, to make half the required quantity, then mixed with an equal weight of melted glycero-gelatin and poured immediately into moulds. A firmer consistence may be secured with water-soluble substances, by substituting mucilage of acacia for a portion of the water or glycerin.

This vehicle makes suppositories containing about 25 per cent of gelatin, and can be employed for any of the medicinal substances used in suppositories. Tannin, alum, etc., mix better with this than with a base containing water, hence no water should be employed for dissolving these. They are soluble in glycerin, and that alone must be employed. If the gelatin hardens when first mixed, continued heating will re-liquefy it. They are not, however, suitable bodies for combining with gelatin.

Softer suppositories can be made by decreasing the gelatin. The same glycero-gelatin mass may be used, but enough glycerin is added to reduce the proportion of gelatin in the finished suppository to even 10 or 15 per cent. Delaye recommends a 7 per cent gelatin for bodies which are soluble in gelatin; an 8 per cent for vegetable extracts and liquid bodies like ichthyol, creolin, etc., and a 10 per cent for hygroscopic bodies, and very soluble bodies, as chloral, iodides, etc. These require longer to set than the larger proportion of gelatin, and should be allowed to remain in the moulds 12 hours.

In certain cases glycerin is too irritating for use, and a hydrated gelatin vehicle must be employed.

L. A. LeMieux prefers the following mixtures:

Formula No. 1.—Gelatin 40 parts, glycerin 25 parts, water enough to make 100 parts.

Formula No. 2.—Gelatin 40 parts, glycerin 25 parts, acacia 25 parts, water 200 parts. Evaporate to 100 parts.

Formula No. 1 is adapted for general use, and No. 2 is suitable for warm or moist atmospheres, or for very hygroscopic bodies.

The moulds should be warmed before pouring, particularly urethral moulds.

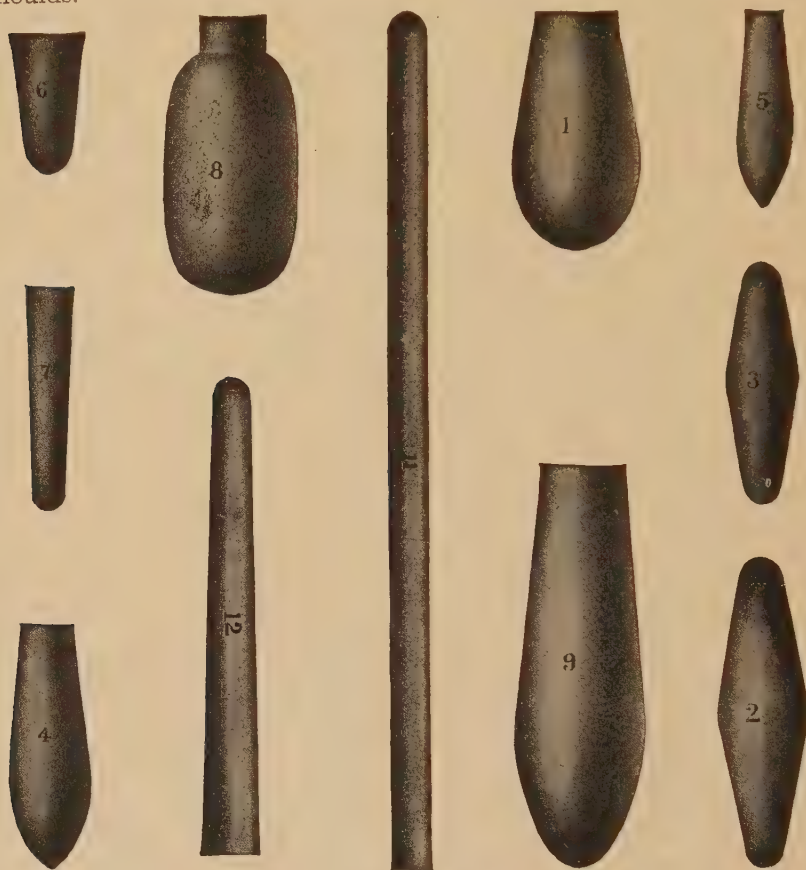


FIG. 56.—Suppository forms.

For extra long urethral suppositories, and for unusual sizes or shapes of other suppositories, moulds made of oiled paper serve excellently. They are formed over a pencil or any convenient object, and when the gelatin has set the paper cover is removed and the suppositories trimmed.

Gelatin suppositories are useful in cases where fats are objectionable, but are not as agreeable to the patient as suppositories made with cacao butter. The gelatin has a rubber-like feel, and clings to the surfaces unless wet with water immediately before inserting; more-

over, it is less quickly absorbed. They should be kept in a *dry* and *cool* place, since they are hygroscopic, and will melt if moistened.

Other Bases.—The three bases mentioned—cacao butter, glycerin-gelatin, and soap—have been found satisfactory in all cases thus far, and there seems to be no demand for others. Many mixtures of common fats and waxes, or of new bodies, have been proposed at various times, but the advantages offered are in nearly or quite all cases offset by corresponding disadvantages, and they have attracted only a momentary attention. Probably the above three bases will continue to be used almost exclusively for many years to come, and the following which have been proposed are mentioned merely as interesting substitutes.



FIG. 57.—Standard size suppositories. (Cacao butter.)

Equal parts of oleic and stearic acids give a mixture for which the following advantages were claimed by Mr. Martindale: It melts at the temperature of the body, shrinks upon cooling, and the suppositories are thus easily removed from the moulds; the suppositories are very firm, and the proportions may be varied to suit varying conditions of temperature, ingredients, etc. It also is an excellent solvent for alkaloids, and is readily absorbed.

This is probably the best substitute for cacao butter that has yet been proposed.

Cocoanut stearin, stiffened with a small proportion of wax, is stated to make a less expensive base than cacao butter. It has a tendency to become rancid, which is objectionable.

A mixture of anhydrous lanolin and stearin is claimed to make an excellent base, which is permanent and more easily absorbed than cacao butter.

For making urethral suppositories (bougies) N. Pritzku, Ph. G., has recommended a mixture made as follows: A troy ounce of cacao butter is melted and mixed with four drachms of powdered acacia, then four fluidrachms of water and two of glycerin are incorporated, and when well emulsified the mixture is chilled. When required for use, the medicinal agent is first incorporated with a little cold cacao butter, then triturated with the above mixture in suitable quantity, and the suppositories are rolled out by the cold process. Dry powders may be mixed with an equal weight of glycerin instead of with cacao butter, before adding the mixture.

A bougie-mass sometimes used for vaginal bougies is made by mixing 6 cc. of glycerin with 6 cc. of water, and pouring this upon 10 Gm. of powdered elm bark, which is then quickly worked into a mass and divided into 6 globular bougies. The mass must be worked rapidly, for it hardens in about ten minutes. After 24 hours the suppositories become hard and elastic; but after being inserted into the vagina they soften and swell, making both a mucilaginous fluid and a distention of the walls. Medicinal agents may be incorporated.

An English pharmacist, J. Cooper, Ph. C., states that he finds calcium oleate of value in preparing suppositories or ointments containing a considerable amount of liquid. The oleate acts by forming a water-in-oil emulsion which is made in the usual manner of emulsions. For suppositories he recommends one grain of calcium oleate to each suppository, to be dissolved in the cacao butter and the liquids stirred in. For ointments he recommends one per cent of the oleate dissolved in the melted base. Such a base, he states, will take up an equal weight of liquid by cold trituration. The calcium oleate is made by precipitating a solution of castile soap with a slight excess of solution of calcium chloride, washing, drying and powdering the precipitate. The powder must be thoroughly dried to render it easily soluble in the fats.

MOULDS

Moulds are of various kinds, the most common being of brass, nickled iron or white-metal.

Those which separate longitudinally are easier to use, rendering the ejection of the suppository much easier.

Two sizes are needed; one for rectal suppositories and one for vaginal. A pessary or urethral mould is also desirable.

All moulds should be standardized for the amount of base which they will hold as soon as received.

They are usually designated as 15-grain, 20-grain, 30-, 45-, 60-, 120-grain, etc., but the amounts which they will actually hold will commonly vary a little from these figures. The beauty and value of the suppository demands that the moulds be well filled, and that none of the mass containing a part of the medicinal agents be wasted, hence the capacity of the mould should be accurately known.

It is more convenient to know the volume-capacity of the moulds, since this will be the same for all bases.

This is quickly ascertained by over-filling the moulds with cacao butter, allowing this to solidify, and after removing all excess of butter remelting the suppositories so obtained. The liquid fat is now

measured in a graduate, or a test-tube which is thereafter kept for that use. Rectal moulds commonly hold four to six drachms of melted cacao butter per dozen suppositories, and vaginal moulds two to four times these quantities.

When a new base or a mixture of bases is used, the quantity necessary for filling the moulds is readily obtained by measure.

A ready means of ascertaining the capacity of a mould is to fill it with water from a pipette, and multiply the number of minims of water required by 0.9 to get the capacity in grains of cacao butter.

Metallic moulds should be kept clean and dry. If allowed to become rusty the surface is roughened and the appearance of the suppository is marred, as well as the difficulty in ejecting it from the mould increased.

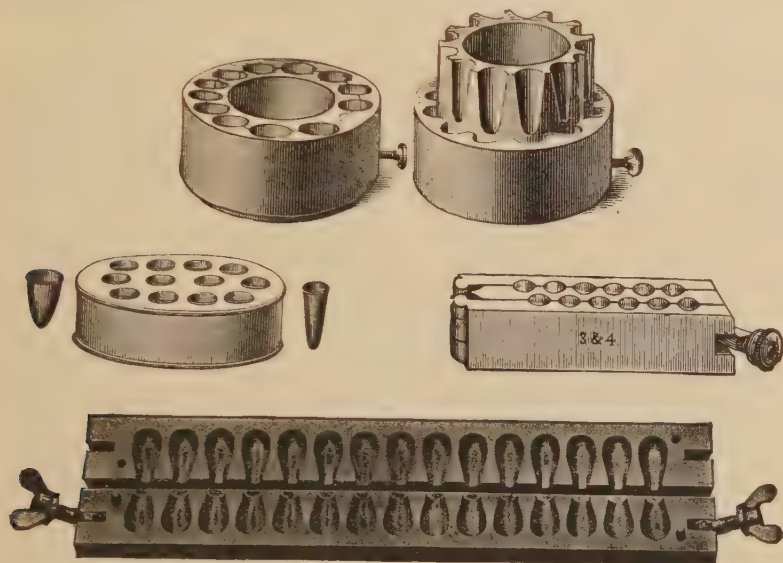


FIG. 58.—Suppository moulds.

Extemporaneous moulds may be made by rolling waxed paper or tin-foil upon a wooden form and then sticking into wet sand. Upon withdrawing the form the paper mould is left in the sand ready for use.

Plaster-of-Paris moulds are made by preparing a thick cream of plaster-of-Paris with water, which is then poured into a suitable box or frame, and suppositories of wax inserted until the plaster hardens.

The wax suppositories are then removed, the edges of the mould smoothed, and the mould rendered less absorbent by boiling for a short time in linseed oil.

Suppository machines or compressors are in common use at present. In these the cold mixture of base and medicaments is placed in a strong cylinder or hopper, and forced by pressure, applied by means of a screw, into the moulds. These make smooth, hard suppositories, and are especially useful in making large quantities.

More care is required in mixing the mass than when the mass is melted and poured into chilled moulds.

THE MANUFACTURE OF SUPPOSITORIES

This is accomplished by three processes, viz., the hot process, the cold process, and by means of a suppository machine or compressor.

In making them by the hot process sufficient cacao butter is first weighed out to just fill the moulds, and about two-thirds of it placed over a water-bath in a capsule or casserole. While this is heating the medicinal ingredients are weighed out and prepared for incorporating with the remainder of the cacao butter.

Powders or salts should be rubbed to an impalpable powder, taking special care that no grit or small lumps are allowed to remain, then mixed thoroughly with the cacao butter which has been reserved.

Extracts should be first softened and rendered semi-liquid by means of a little water or diluted alcohol, then incorporated with the reserved cacao butter.

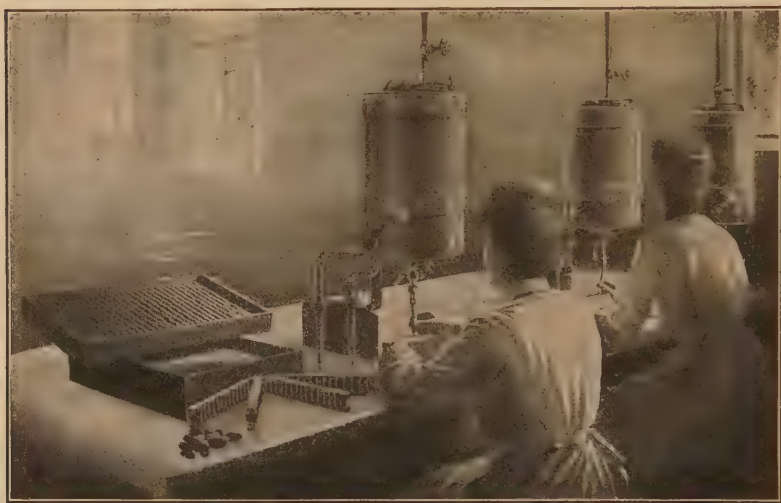


FIG. 59.—Making gelatin suppositories.

In the meantime the cacao butter which was placed in the capsule has melted, and the capsule containing it should be removed from the heat and its contents allowed to cool to 95° F., or lower, then the medicated butter, now rendered soft by friction, is added to that in the capsule, where a little stirring with a spatula or glass rod will render the whole liquid and homogeneous.

The fluid is now poured into the chilled moulds and the moulds allowed to remain on the ice until the suppositories have hardened.

The temperature at which the mixture is poured into the moulds is the critical point with most suppositories. If too hot, insoluble salts will settle at the apex of the suppositories before the mass stiffens sufficiently to hold them in suspension. Extracts, particularly extracts of belladonna, stramonium and hyoscyamus, are precipitated in granular condition by the least excess of heat and cannot again be reincorporated, while volatile bodies, alkaloids, etc., may be driven

out or decomposed by the heat. The mass shrinks on cooling, and if poured while hot, a depression forms at the top of the suppository, which is unsightly.

Moreover, the suppositories are more easily removed from the moulds and consequently less liable to break if the mass has begun to thicken before being poured.

A little practice will enable one to judge of the proper temperature of the melted butter without the use of a thermometer.

The capsule will not feel warm to the hand, and the butter will show signs of thickening. If the medicinal agents and the cold cacao butter be triturated vigorously just before it is added to the melted butter, it will become softened by the friction and liquefy the more readily.

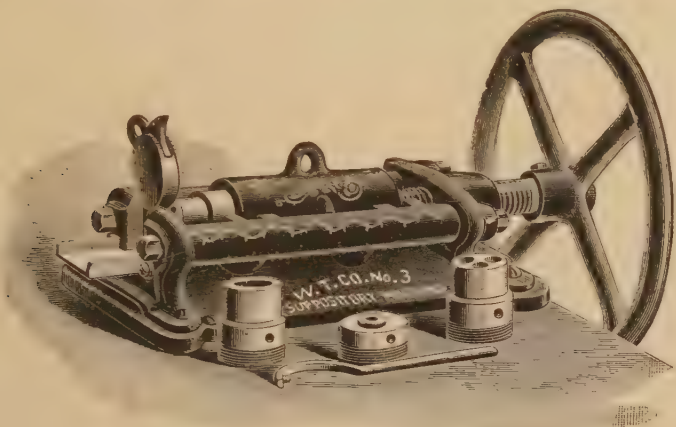


FIG. 60.—Suppository compressor.

Should a little additional heat be necessary it must be applied cautiously.

A momentary application to the water-bath, then a brief stirring with a glass rod, and the process repeated if needed, will suffice and will avoid overheating.

It should be remembered that in the melting of any solid body latent heat must be absorbed, and if done rapidly the portion first melted will become heated far beyond its critical point before the last portions of the solid become liquefied, hence the necessity of first melting a portion of the cacao butter and allowing this to cool before adding the medicinal agents.

Some pharmacists favor the **sprinkling of the moulds** with lycopodium. This was formerly sanctioned by the Pharmacopœia, but is usually not necessary if the moulds be well chilled before pouring in the mass.

Some prefer to use a little fixed oil or petrolatum rather than lycopodium, while soap-liniment is favorite with others.

The latter should never be used for suppositories containing metallic salts, lest a reaction occur between the soap and the salt. An alcoholic solution of castor oil is a good substitute in these cases.

Still another way of preventing sticking is to line the moulds with tin-foil or waxed paper.

The moulding of urethral suppositories is often troublesome. If the moulds are well chilled the mass will often congeal before reaching the bottom of the mould, leaving a portion unfilled.

The better way is to pour the mass into the moulds before completely chilling, then chill thoroughly, and after the mass has congealed remove from the ice and allow to stand until the mould has acquired the temperature of the room again.

This is necessary because, in chilling, the metal of the mould contracts more than the cacao butter, and grips the suppository tightly when very cold. Upon allowing the mould to warm in the air, the metal expands and allows the suppository to slip out.

Extemporaneous urethral moulds are best formed of tin foil or waxed paper. They are especially convenient for making gelatin bougies of different sizes.

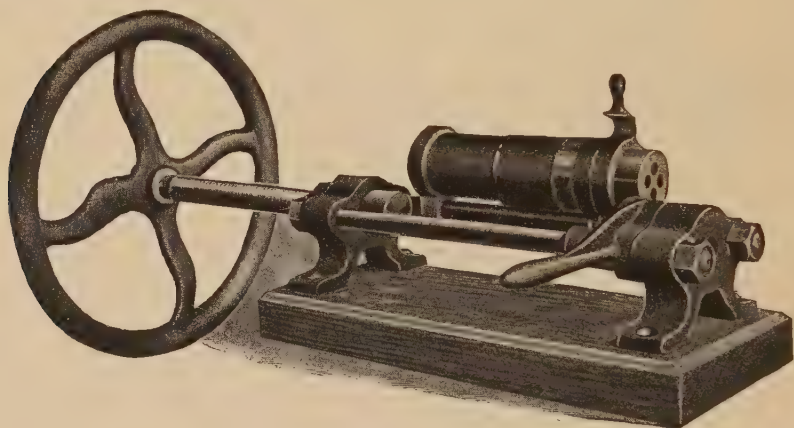


FIG. 61.—Suppository machine.

A glass tube rounded at the end, and not entirely closed, makes an excellent form. The suppositories should be made 2 to 2 $\frac{1}{2}$ inches long and $\frac{1}{8}$ to $\frac{1}{4}$ inch in diameter. The waxed paper or foil having been wrapped smoothly around the glass tube, the tube is then gently withdrawn, the air-vent in the end allowing of its easy removal, and the shell makes an excellent mould. It will be found difficult to remove the shell from a pencil, if substituted for the glass tube, owing to suction of the air.

In pouring the melted mass from a dish into the mould, there is a slight loss due to the adhesion of the melted fat to the dish, and unless considerable care is exercised the dispenser may not be able to fill the last mould. The size of the dish has much to do with this, as also care in manipulating. But good dispensers allow for this loss by making an extra quantity of mixture. Thus, if a dozen suppositories are desired, enough mixture is made for thirteen suppositories, and twelve are poured. This insures a full and accurate dose of medicinal agent in each suppository.

In the absence of ice the moulds may be chilled by spraying ether upon their surface from an atomizer. The rapid evaporation of the ether quickly chills the metal as effectually as when ice is used. Only a little ether is needed. Carbon disulphide, benzine, chloroform and other easily volatilized liquids can be used in the same way.

Another method is to cool the mould in a "freezing mixture," obtained by quick solution of a salt in water.

The mould is three quarters submerged in water in a suitable vessel, then a definite proportion of some quickly dissolving salt is stirred in, which lowers the temperature of the water as it passes into solution and thus chills the mould. If the suppositories do not harden readily two such treatments may be necessary, one for the preliminary chilling and one after the moulds have been filled. In many cases the salt may be divided, and one portion used for the first chilling, while the other is reserved for use in the second. For instance, if the mould be put into a dish containing not more than 14 fluidounces of water, then 2 ounces of ammonium nitrate added and quickly dissolved by stirring, the mould will be cooled enough for the pouring. Then as soon as the moulds are filled, 2 ounces more of ammonium nitrate are added, and suffice for the hardening of the suppositories. The solution may afterward be evaporated and the salt recovered for subsequent use.

The following table gives a list of salts suitable for this purpose, and the proportions by which the lowest temperature is obtained.

LOWERS THE
TEMPERATURE

Ammonium nitrate 1 part, water 1 part.....	27° C.
Ammonium chloride 1 part, potassium nitrate 1 part, water 1 part.....	35° C.
Potassium sulphocyanide 5 parts, water 4 parts.....	33° C.
Glauber's salt 8 parts, hydrochloric acid 5 parts.....	27° C.
Sodium phosphate 9 parts, diluted nitric acid 4 parts.....	39° C.

The salts should be finely powdered, used in just the above proportions and quickly stirred, in order to obtain the above results. The limit of temperature depends upon the degree started with and the limit of solubility.

The cold process is preferred by many, even when a compressing machine is not available and the suppositores have to be formed by hand, being more sure of success, and often more quickly finished. For this method the entire amount of cacao butter should be grated or shaved, and then mixed with the medicinal ingredients in the same way that a pill-mass is worked.

A little castor oil or glycerin is worked in, about a drop to each suppository, to render the mass more cohesive. After working the mass in a mortar until it has become homogeneous and plastic (taking care that no particles of cacao butter show in the mass), it is taken out and worked in the hands or on a pill-tile until formed into a cylinder. It is then cut into the required number of pieces, and each piece formed into a conical (or otherwise) suppository, by means of the fingers and a broad spatula. Dunning's mixture (page 264) works well for the cold method.

Practice is required in this method in order to work rapidly, and make smooth and even suppositories, but the skill is easily acquired and the process gives satisfaction.

If the mass begins to break, its plasticity may be restored by working thoroughly in the hands. On the other hand, if handled too much the mass begins to melt. Deftness is the whole secret of this operation.

In warm weather or in a warm room it may be necessary to cool the hands from time to time by immersing them for a moment in ice water and wiping quickly.

The pill-tille should be kept well dusted with lycopodium or starch while working the mass upon it. Starch is to be preferred in most cases.

When a compressing machine is used, the mass is made in the same manner, then placed in the cylinder and forced into the moulds. Suppositories made in this way look much like those by the hot process.

The machine and moulds should be thoroughly cleaned after each mass, or succeeding lots may appear streaked.

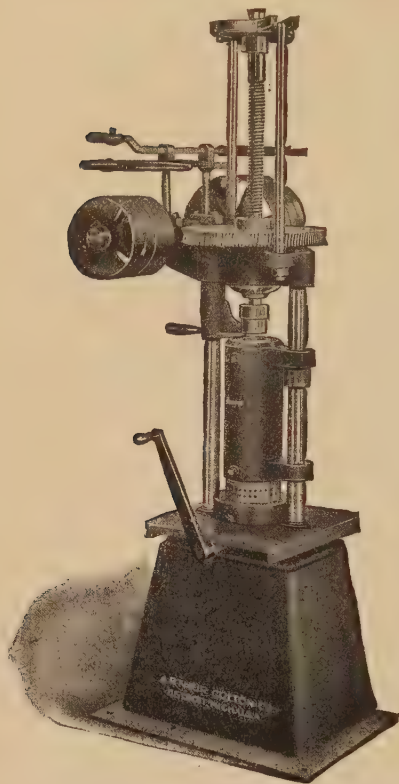


FIG. 62.—Power suppository machine.

COATING SUPPOSITORIES

Suppositories containing hygroscopic substances, as glycerin, or very volatile bodies, are sometimes protected by coating or wrapping them.

Flexible collodion, paraffin, and wax are used as coatings. The suppositories are impaled upon needles and dipped quickly into the collodion or melted wax, then set aside until the coating has hardened.

These are good protective agents, but have been objected to because patients frequently neglect to remove the coating before inserting the suppository, and it does not melt or absorb, as intended. When dispensed with coatings, plain directions for the removal of the films should be affixed to the container and verbal instructions also given to the patient.

Similar protection is afforded by wrapping the suppository in tin-foil or paraffined paper. It is generally preferred, however, to dispense such as need be protected from the air in tightly stoppered bottles or in glass tubes containing only one or two suppositories.

Politzer Plugs are allied to bougies, in that they are made for insertion into the meatus of the ear for protection. They are not medi-

cated, but are intended only for protecting the inner ear after surgical operations, or for special reasons. They are made of greased cotton in the following manner: A small pellet of absorbent cotton is first pierced with a thread so that it will hang from about two inches of the double thread. With the fingers, the cotton is thoroughly greased with simple cerate and made into a pellet about the size of a coriander seed. When well greased, a thin layer of fresh cotton is folded smoothly over it, and the latter is greased with the ointment in turn. Then another layer of cotton is put on and greased in its turn, and the process is continued until a ball is made which will fill snugly the meatus of the ear and exclude the air without distending it or causing discomfort. Varying sizes will be needed to fit the patient.

When inserted, the thread is left hanging out and is utilized for removing the plug from the ear.

The innermost pellet of cotton needs but a little greasing and should not be made into a hard ball, but the outer layers must be thoroughly greased and put on firmly. This makes a plug which is firm on the outside, but a little elastic and so fits the meatus of the ear snugly. The thread can be put into the plug after it has been formed if desired.

Dispensing.—Suppositories should be sent out in tight boxes lined with impervious paper. Special compartment boxes are employed so that the suppositories do not come in contact with each other. These are to be preferred; but plain, well-lined boxes may be employed, the suppositories being wrapped in waxed paper or tin-foil. If the suppositories are soft, a little starch or lycopodium may be sprinkled upon them. It is not necessary to bury them in powder. In all cases a label upon the box directing its storage in a cool place is almost a necessity.

SUPPOSITORIES

I

- R. Glycerin..... 80 Gm.
 Monohydrated sodium
 carbonate..... 2 Gm.
 Stearic acid..... 8 Gm.
 Water 10 cc.....
 M. s. a. Make ten rectal supposito-
 ries. Sig.—Glycerin suppositories,
 U. S. P.

Dissolve the sodium carbonate in the water and add it to the glycerin in a flask on a water-bath; then add the stearic acid, and heat carefully until this is dissolved, the escape of carbonic acid gas has ceased, and the liquid is clear. Then pour the melted mass into suitable moulds, remove the suppositories when they are cold, and wrap each in tin-foil.

Make one-third the quantity and pour into vaginal moulds.

2

- R. Acidi stearic..... 0.250
 Sodii carbonat. exsic..... 0.250
 Glycerini..... 9.500
 M. Ft. supposit. no. v. Sig.—
 Transparent glycerin suppositories,
 95 per cent.

3

- R. Gelatin..... 2 Gm.
 Glycerin..... 10 Gm.
 Distilled water..... q. s.
 Make six rectal suppositories.
 Sig.—Glycerin suppositories, Ph. Br.

Place the gelatin in a weighed evaporating dish with sufficient water to cover it, allow it to stand 15 minutes, then pour off the excess of water; set aside until the gelatin is quite soft, then add the glycerin. Heat on a water bath until the gelatin is dissolved and the mixture has been reduced by evaporation to 13 grammes, and pour into moulds.

4

- R. Camphoræ..... 2.00
 Olei theobromat..... q. s.
 M. Ft. supposit. vj no. pro recto.
 Sig.—“Camphor suppositories.”

Dissolve the camphor in the melted butter and pour the solution into the moulds.

5

- R. Extracti belladonnæ..... 0.100
 Morphinae sulphatis..... 0.100
 Olei theobromatis..... q. s.
 M. Ft. suppositoriæ pro recto vj no.
 Sig.—Morphine and belladonna.

6

- R. Iodoformi..... gr. vj
 Acidi tannici..... gr. xij
 M. Ft. supposit. pro recto vj no.
 Sig.—“Iodoform and Tannin suppositories.”
 (Caution: Avoid overheating these.)

7

- R. Mitte Suppositoriæ Iodoformi pro recto aa gr. ij no. vj.
 Make by two methods.

8

- R. Plumbi acetat..... 1.20
 Pulv. opii..... 0.40
 Olei theobromatis..... q. s.
 M. Ft. supposit. pro recto vj no.
 Sig.—“Lead and opium suppositories.”

9

- R. Chloralis..... 2.00
 Olei theobromatis..... q. s.
 M. Ft. suppos. pro recto vj no.
 Sig.—“Chloral Suppositories.”

For cold process, powder the chloral, incorporate with cacao butter and form into suppositories.

For hot process, melt 1.5 Gm. spermaceti. Mix with 5 Gm. of warm cacao butter, dissolve the chloral in the warm (not hot) mixture, add enough cacao butter to make up to the full volume of the moulds (3 iiss), mix well and pour into the chilled moulds.

10

- R. Extracti belladonnæ..... 0.187
 Morphinae sulphatis..... 0.130
 Olei theobromatis..... q. s.
 ut. ft. suppositoriæ pro
 vagina sex numero.
 Sig.—Morphine and belladonna.

Make by mould and by hand.

11

- R⁴ Unguent. hydrarg. 2.0 Mix the ointment thoroughly with
 Olei theobromatis. q. s the melted butter and pour into well
 M. Ft. supposit. vj no. chilled moulds.

12

- R. Ext. carnis. 3 j
 Pepsini. 5 ss
 Pancreatini. 3 ss
 M. Ft. suppos. vj no.
 Sig.—Nutrient suppositories.

13

- R. Paraldehyd. 5 iij Add half a drachm of spermaceti and
 Oli theobromat. q. s. q. s. cacao butter. If made by the cold
 M. Ft. suppositoriæ pro recto vj no. process, melt the spermaceti, allow to
 Sig.—Use when needed. partially cool, stir in the paraldehyde,
 allow to solidify, then incorporate with
 the cacao butter.

14

- R. Iodoformi. 1.000 When a prescription calls for a num-
 Olei eucalypti. 0.250 ber of suppositories that are liable to
 M. Ft. suppositoriæ pro urethra iij no. give trouble in moulding, if the material
 is not too expensive it is well to attempt
 to make more than the number called
 for in the hope of securing the required
 number in satisfactory condition at
 once. In this case attempt double the
 number, using equal parts of spermaceti
 and cacao butter as a base.

15

- R. Acidi tannici. 0.187 Use cacao butter for hand method,
 Acidi carbolic. 0.187 and one-third spermaceti for hot
 Olei theobromatis. q. s. process.
 M. Ft. suppositoriæ pro urethra iij
 no.

16

- R. Camphoræ. gr. viij
 Chloralis. gr. viij
 Cetacei. 3 ss
 Olei theobromatis. gr. xv
 M. Ft. pessarium.
 Sig.—Headache discs.

17

- R. Iodoformi. gr. xx
 Bismuthi subnit. gr. xx
 Olei theobromatis. q. s.
 M. Ft. suppos. vj no.
 Sig.—Use one 3 times daily as
 directed.

18

- R. Salol. 2.0 If the cacao butter is heated enough
 Olei theobromatis. q. s. to melt the salol when mixed (42° C.),
 M. Ft. suppos. vj no. the mixture will not harden readily.
 Sig.—Salol suppositories.

19

- R. Acidi borici. 7.5 Dissolve the gelatin in the water by
 Gelatini. 15.0 heat, add the glycerin and boric acid,
 Glycerini. 62.5 and, when clear, pour into moulds.
 Aquæ. 15.0
 M. Ft. suppos. xl no.
 Sig.—Boroglycerin suppositories.

- 20
- R. Gelatini glycerinati..... 20
 Glyceriti boroglycerini..... 15
 Glycerini..... 15
 Misce ft. suppos. recto xii no.
 Sig.—Boroglycerin suppositories.
- 21
- R. Suppositoriæ pro vaginæ
 Ichthyol, 10 per cent. . . . No. xx.
 The ichthyol is not well taken up by wax. Mix the ichthyol with sufficient starch to absorb it, add sufficient cacao butter and make by the cold process. If moulded the mass is aided by mixing the ichthyol with half its weight of water, then using 10 per cent of beeswax in the cacao butter.
- 22
- R. Ichthyol..... 3 iv
 Chloretone..... gr. xxiv
 Thymol iodid..... gr. xv
 Ol. theobromat..... 3 v
 M. Ft. suppos. no. xii.
- Mix the ichthyol and chloretone with about an equal weight of powdered soap before incorporating.

Prescriptions from State Board Examinations

FOR CRITICISM AND PRACTICE

- I
- R. Iodoformi,
 Pulvis opii.....aa gr. xii
 Pulvis camph..... gr. iii
 M. Fac suppositorias cum olei theobromatis vi no.
 Sig.—One at night as directed.
 (Tex. and Ill.)
- 2
- R. Ext. belladonnæ..... gr. 1/4
 Acidi carbolicci..... gtt. ii
 Olei theobromat..... q. s.
 Fiat. suppos. i. no.
 Mitte vi.
 Sig.—One at night. (Ill.)
- 3
- R. Extracti belladonnæ..... 0.02
 Thymolis iodidi..... 0.06
 Olei theobromatis..... q. s.
 M. Ft. suppos. d. t. d. vi no.
 Sig.—Unum omni tertia hora.
 (N. Y.)
- 4
- R. Pulv. opii..... 0.03
 Ol. theobrom..... 12.00
 M. Ft. suppos. d. t. d. vi no.
 Sig.—One every 6 hours. (N. Y.)
- 5
- R. Acid tannici..... gr. x
 Ext. bellad. alc..... gr. v
 Ol. theobromat..... q. s.
 M. et in suppos. vi divid.
 Sig.—More dict ac nocte injec. (Br. Col.)
- 6
- R. Acidi tannici..... 1.0
 Pulv. opii..... 0.2
 Olei theobrom..... q. s.
 M. Ft. suppos. vi no.
 Sig.—As directed. (N. Y.)
- 7
- R. Sulphuris præcip..... gr. xxx
 Ol. theobromatis..... q. s.
 M. et fiat suppos. iii no.
 Sig.—One suppository at night.
 (Ill.)
- 8
- R. Camphoræ..... 2.0
 Olei theobromat..... q. s.
 M. Ft. supposit. vi no. pro recto.
 Sig.—Camphor suppositories.
 (Mass.)
- 9
- R. Acid tannici,
 Plumbi acetat..... aa gr. xv
 Ext. belladon..... gr. x
 Ol. theobrom..... q. s.
 M. Ft. suppos. x. no.
 Sig.—Ut. dict. (Tex.)
- 10
- R. Iodoformi
 Pulv. opii.....aa gr. ii
 Pulv. camphoræ..... gr. iii
 Ol. theobromæ..... q. s.
 M. et fiat suppos. vi. no.
 Sig.—One at night as directed. (Fla.)
- 11
- R. Extracti belladonnæ..... 0.01
 Olei theobromatis..... 4.00
 M. Ft. suppositoria rect no. vi.
 Sig.—One as directed. (N. Y.)

CHAPTER XIII

OINTMENTS, CERATES, PLASTERS

Ointment (Lat. *Unguentum-i*).—A fatty preparation of such a consistency as to be easily applied to the skin by inunction, gradually liquefying when in contact with it. (Cent. Dict.)

Cerate (Lat. *Ceratum-i*).—A fatty preparation resembling an ointment, but having a firmer consistency and a higher melting-point. True cerates always contain wax (Cera).

Salve (Lat. *Christma, atis*).—A stiff ointment or cerate to be applied to wounds or sores.

Unguent.—A term applied mostly to perfumed salves or ointments used for anointing or for toilet purposes.

Plaster (Lat. *Emplastrum-i*).—A solid compound intended for external application, adhesive at the temperature of the human body, and requiring to be softened by heat before being spread. (Cent. Dict.)

Pomade (Lat. *Pomatum-i*).—A fat saturated with the odorous principles of plants by enfleurage; or a perfumed ointment or cerate used for the scalp and in dressing the hair.

These differ chiefly in their consistence and melting-points, the ointments being soft unctuous solids, which should partially melt when applied to the skin, the cerates stiffer, and having a slightly higher melting-point, and the plasters have just enough pliability to adhere to the skin, and offer a slight mechanical support and protection, as well as a medicative action through the absorption of medicinal matters contained therein.

They, with the true liniments, afford a gradation from the fluid oil-bases to the stiff waxy or resinous bases, any desired consistency and melting-point being obtained by mixtures of the oils, soft fats, waxes, and resins. They are all designed to produce an effect through the absorption of medicinal ingredients, in which they differ from the plasmas, which are designed for purely external or surface effects, medicinal matter not being absorbed from them to any extent.

Constitutional effects are often produced by the thorough rubbing-in of liniments or ointments, applied usually to the axillæ or groin, where the medicinal matters are more quickly absorbed.

Mercurials, narcotics, etc., can be made to produce their effects upon the system in this way, just as thoroughly as when taken by the mouth.

Professor C. S. N. Hallberg classified these preparations therapeutically as:

1. **Epidermatic.**—Those which are intended to act only upon the surface of the skin. These are non-absorbent, and include such ointments and plasters as act as protectors, antiseptics, astringents, counter-irritants, germicides, and parasitocides. The best vehicle for these is petrolatum and paraffin.

2. **Endermatic.**—Those which are intended to penetrate *into but not through* the skin. These are semi-absorbent, and include such as act as emollients, anodynes, alteratives, resolvents, sedatives, stimulants and local irritants. The best vehicles for these are the vegetable oils and true fats, as lard, suet, almond or olive oil, etc.

3. **Diadermatic.**—Those which are intended to pass through the skin and produce constitutional effects. These are somewhat rare, and include *special uses* of mercurials, iodides, belladonna, conium, etc. The best vehicle for these is lanolin, or wool-fat, though cacao butter is also used.

Care must be taken to discriminate between the uses of these vehicles, particularly not to employ pure wool-fat when a systemic effect is not desired. But in combination with petrolatum the very absorbent powers of wool-fat are reduced, and a mixture of equal parts of petrolatum and wool-fat corresponds closely, in therapeutic properties, to lard and the endermatic vehicles.

In a report to the Science Committee of the British Medical Association (Br. Med. Jour., July, 1911, and October, 1913) Dr. Robert D. Wild reviews the various bases and describes their peculiarities. From a therapeutic standpoint the melting-points, absorptive properties, and consistency and adhesiveness of an ointment are important and therapeutic failures may result from a mistake in the selection of the base.

An ointment should spread easily and smoothly, so as not to cause pain upon a tender surface, should be adhesive, and should soften gradually below its melting-point. For the last qualification a mixture of fats is often better than a single fat having a sharp melting-point.

The absorption of an ointment is not altogether due to its fatty constituents, for all medicinal agents do not absorb in the same way. Thus F. Samlan says that iodine and methyl salicylate are absorbed most rapidly from a petrolatum base, while other salicylates are absorbed most rapidly from lard or wool-fat.

In general petrolatum is the best base for protective or epidermatic ointments, while wool-fat and lard are better for endermatic or diadermatic ointments.

Dr. Wild reports that ointment of ammoniated mercury made with lard accomplishes its purpose in two-thirds the time of one made with petrolatum.

OINTMENTS AND CERATES

The usual bases for these are lard, lard and wax, petrolatum and wool-fat. Oils stiffened with wax or paraffin have been used, but possess no special advantages, and are rarely ordered. Frequently the medicated jellies or glycono-gelatins are termed ointments. These are treated in the chapter on Plasmas.

The three principal bases, lard, or lard and wax, petrolatum and wool-fat, differ widely in character, both medicinally and pharmaceutically.

Each has the property of absorbing or emulsifying small quantities of water, but in different degrees, and they also vary in their absorbability and the promotion of medicinal action.

Lard (Lat., *Adeps*, gen. *Adipis*) is the prepared internal fat of the abdomen of *Sus Scrofa*, or hog, purified by washing with water, melting and straining. Much of the lard of commerce is not the abdominal fat, but the fat of the entire body of the hog, and differs from the official product in melting-point and consistence.

The abdominal lard, which should be used exclusively in pharmacy, is sold under the name of "pure leaf lard." This is sufficiently pure for making ointments, etc., but care should be taken that it does not contain salt or any excess of water.

When exposed to the air, lard soon begins to decompose and becomes rancid. This gives it a strong and disagreeable odor, renders it incompatible with some chemicals, and causes an irritation when it is applied to the skin.

The tendency to become rancid is promoted by moisture and heat, and by contact with metals, so to guard against this the lard, and the ointments containing it, should be as nearly anhydrous as possible, and should be stored in glass, in a dry and cool place. To still further preserve it, the Pharmacopœia directs it to be saturated with benzoin, the volatile and antiseptic principles of which are soluble in the melted fat, and these retard change.

The best lard for pharmaceutical purposes is prepared directly from the leaf or flare.

Mr. A. W. Gerard gives the following directions for preparing a superior article: "Cut and bruise 100 parts of fresh leaf (deprived of its outer membrane) and heat in a deep vessel at 55° C. until the fat has melted and separated from its tissues. Add to the melted fat 6 parts of crushed benzoin, and continue to heat and stirring for twenty minutes. Finally strain, and gently press through flannel." If the leaf is bloody or otherwise dirty it should be washed and dried as thoroughly as possible before heating. The addition of a small piece of elm bark while melting aids in clarifying.

By trying out and benzoinating the lard in one operation freshness and sweetness are assured, and the ill-effects of a double heating avoided. A finely fragrant base is obtained by the above process, which is devoid of irritating properties and keeps well. Moreover, it demands little more labor than the official method of benzoinating a prepared lard.

The official method of benzoinating is to suspend the benzoin, coarsely powdered and tied in a muslin bag, in the top of the melted fat, and allow the hot fat to act upon it for two hours. It is more satisfactory to first mix the benzoin with an equal bulk of clean sand, thereby preventing its lumping together in the lard. Siam benzoin gives superior results, and is well worth its cost.

Several quick methods of benzoinating have been proposed, as the incorporating of a concentrated alcoholic or ethereal tincture, or an oil solution, made by dissolving two ounces of benzoin in four ounces of ether and evaporating the filtered solution in an ounce of castor oil, which may then be incorporated with the lard or with extemporaneous ointments.

When lard is incorporated with beeswax or resin, these act as preservatives, and benzoinating is less necessary. One per cent of resin is stated to be quite effective as a preserving agent. An easy test for rancidity is to make an ointment of potassium iodide without any hyposulphite of soda. If the lard is at all rancid, the ointment will become discolored in a short time.

Lard possesses the property of absorbing or emulsifying quite a proportion of water, 100 parts of lard, when cold, emulsifying 15

parts of water, and 100 parts of benzoinated lard taking up 17 parts of water, no other agent being necessary. This is a valuable property from a pharmaceutical standpoint, since it permits of the incorporation of soft extracts or aqueous solutions of salts.

Lard also yields up for absorption the medicinal agents which have been incorporated with it, and is therefore oftentimes preferred when a prompt and strong action is desired. These two valuable properties suffice to hold it in the first rank among the bases, in spite of its objectionable tendency toward rancidity.

Lard slowly reacts with metallic oxides, forming an oleostearate of the metal. This is the reason for the granulation of the former official zinc oxide ointment which was made with lard. Petrolatum does not so react.

The mixtures of lard and water are subject to the usual incompatibilities of emulsions, and it is rarely possible to incorporate as much of a saturated salt solution as of pure water. The range is wide enough for most purposes, however, and evaporation usually aids in incorporating troublesome fluids.

Petrolatum is the most unchangeable of the bases, being unacted upon by air, moisture or chemicals. When of a good quality, it is inactive in itself, but the commercial grades sometimes contain some acid, used in purifying and bleaching, or other oxidation products which are irritating.

It may be obtained of almost any consistence and fusing point—from the liquid petrolatum to the hard paraffin wax, melting at 45° to 65° C. These are all similar in nature and composition, being derived from petroleum or "rock oil." They are useful as solvents, but do not mix well with aqueous fluids.

One hundred parts of petrolatum will absorb 5 to 10 parts of water.

It does not yield up for absorption medicinal agents very readily, and is hence adapted for ointments which are designed to act upon the surface only.

It is almost the opposite of lard, being permanent under ordinary conditions, taking up but little aqueous or alcoholic fluid, and usually retarding absorption.

The most troublesome feature in the use of petrolatum pharmaceutically is the difficulty of combining aqueous fluids with it. Thus it is unsuited for the preparation of such ointments as potassium iodide, etc. Many plans for overcoming this have been proposed, the best of which is the addition of yellow wax. Petrolatum containing 5 per cent of yellow wax will absorb (or emulsify) 3 to 4 times as much water as pure petrolatum.

Petrolatum containing 3 per cent of cholesterol absorbs liquids quite readily, and has been especially recommended for eye ointments. It has also been suggested as a substitute for wool-fat, being less sticky and almost odorless. It is not as absorptive of liquids as wool-fat.

Wool-fat (*adepts lanæ*) is the purified fat of the wool of sheep, and occurs either in anhydrous form or containing 25 to 30 per cent of water. Both the anhydrous and hydrous forms are official. It is not a pure fat, but a mixture of several fats with certain organic acids, esters and cholesterol, or waxy alcohols.

It is a tough, unctuous solid, not as easily worked as other fats, but capable of dissolving or emulsifying an equal weight or more of water, and it does not easily become rancid. If exposed freely to the action of light, air and moisture, after several months it begins to decompose; but under ordinary conditions it will keep for a long time without a trace of rancidity. It is stated to be aseptic.

It is very quickly and freely absorbed by the skin, being very similar in character and composition to the fatty matter secreted by the sebaceous glands of the human body.

It affords a very useful vehicle for incorporating large proportions of liquids in ointments, suppositories, etc., but is not a good vehicle for the incorporation of insoluble powders or bulky solids.

Its stickiness is also objectionable.

This stickiness is partly overcome by the addition of a small proportion of petrolatum. A mixture which has been proposed as particularly free from stickiness is: anhydrous lanolin, 65 parts; liquid petrolatum, 30 parts; ceresin, 5 parts; water, 30 parts. The ceresin is melted and stirred into the liquid petrolatum, then this mixture is added to the anhydrous lanolin, and finally, the water is incorporated.

Dr. Eugene Unna ascribes the liquid-absorbing properties of wool-fat to higher alcohols of the ischolesterol and oxycholesterol groups which have been separated and put upon the market in Germany under the name of eucerin wax.

Eucerin, like wool-fat, is marketed in the anhydrous form, as an unctuous, pale yellow mass of petrolatum-like consistency and not sticky; in the form of hydrous eucerin it is softer. The anhydrous eucerin will absorb about 7 times its weight of water, but when mixed with petrolatum it imparts to the mixture a remarkable absorptive power. Thus a mixture of 5 parts of eucerin and 95 parts of petrolatum is said to be capable of absorbing 500 times its weight of water and to be stable in its keeping properties.

Such a base is especially recommended for a cold cream, but it is stated to promote absorption of medicinal agents equal to wool-fat. The advantages of eucerin are stated to be good consistency, freedom from rancidity, freedom from stickiness, great absorbability, and the promotion of absorption into or through the skin. It has been urged upon pharmaceutical manufacturers, but has not been adopted to any appreciable extent.

Other bases which are commonly associated with the preceding as diluents or stiffening agents are:

Butter fat absorbs 15 to 20 per cent of water and makes a pleasant cooling application. It melts below the temperature of the body, and so makes ointments having a tendency to run when applied. In spite of this ointments made with it rub well. It is the best base for the preparation of citrine ointment.

Oleomargarine has been used for ointments with some advantages. It is firmer than butter and resembles lard in its applications.

Cocoanut fat is especially adapted to ointments for use on the scalp, because it liquefies promptly when applied, and spreads freely on the skin, yet makes a firm ointment of good keeping properties. It is absorbed readily and does not cake on the skin, thus making the

patient more agreeable to its use. It is used largely in liquid preparations for the hair, and has equal virtues as an ointment base for hairy parts.

Beeswax (*Cera*) either bleached or unbleached. White wax usually contains a little foreign fat, and this is frequently rancid and causes the lard in ointment to become rancid also. Beeswax melts at 62° to 65° C.

Much of the commercial beeswax is not a pure wax but consists of a mixture of beeswax and ceresin. It is firmer than pure wax, but has about the same melting-point.

Suet (*Sevum*), the abdominal fat of the sheep purified in the same manner as lard. This is much firmer than lard, and does not become rancid as easily. Suet melts at 44° to 50° C.

Spermaceti (*Cetaceum*) is a crystalline wax-like substance obtained from the head of the sperm whale. It becomes yellowish and rancid on long exposure to air. It melts between 42° and 50° C.

Resin or Colophony (*Resina*), also called "rosin," is a sticky solid obtained as a residue from the distillation of oil of turpentine.

Its melting point varies, usually above 100° C.

Paraffin or waxy petrolatum, white, hard, and melting at 45° to 80° C.

Ceresin or earth wax is a mineral wax obtained from ozokerite and resembles paraffin, but is harder and makes smoother ointments when mixed with fats. It melts from 45° to 68° C. thus varying in its consistency.

Carnauba wax or Brazil wax is the hardest of the waxes, melting at 85° C. It resembles beeswax in general properties but makes a firm ointment in much smaller proportions. A mixture of 10 to 15 parts of carnauba wax with 85 or 90 parts of petrolatum makes an excellent base of good consistency and fair absorbability for protective ointments. **Candellila wax** is very similar.

Besides these, other fats are sometimes called for in domestic practice which are supposed to possess peculiar virtues. Goose-grease is readily absorbed and popular for inunction. Dr. Gardner says it is absorbed more quickly than lard.

Mixed with one-sixth its weight of cacao butter it makes a firm base.

Skunk oil, bear's grease, porpoise oil, rabbit fat, rattlesnake oil, and many others of like character are similar in chemical properties, but are superstitiously regarded.

Artificial fats, consisting mostly of the mono- or di-glycerides of fatty acids (natural fats and oils are tri-glycerides) appear at intervals in the market under the all-inclusive name of "*Ointment Base*." They may be prepared by heating glycerin with mono- or dichlorohydrin and the fatty acid. One or two molecules of the hydroxyl radicals in the glycerin is replaced by the fatty acid, and an artificial fat results. They are usually soft, fatty-appearing bodies which absorb liquids readily. This absorptive property is the item which is usually emphasized in offering them as substitutes for other ointment bases. But while soft in consistency, they do not melt readily, and the high melting point is a decided objection. One sample examined was almost as soft as petrolatum, but did not melt on the water-bath. On keeping this sample shrunk and became harder and more wax-like.

It also darkened in color. The composition of these bases is not disclosed, but they are probably in the main artificial fats.

Starch is used to stiffen ointments and make them more salve-like without raising the fusing-point. It is employed mostly in ointments having petrolatum for a base and insoluble powders as the active medicament, as zinc oxide. It also promotes a closer adherence of these to the skin.

Unna's paste (see page 316) is highly recommended for ointments of salicylic acid, boric acid, lead subacetate, sulphur, phenol, tar, resorcinol, etc.

Superfatted soaps (*i. e.*, soaps containing an excess of oil or fat) have been proposed as bases, the advantages being their freedom from rancidity and from irritating properties, good keeping qualities, ready admixture with medicinal matter, and easy removal from the skin by warm or cold water. The following illustrate them:

Petroxolin—ammonium oleate with liquid or solid petrolatum—a line of which is official in the National Formulary.

Mollin is the name applied to a base prepared by saponifying, without heat, 100 parts coconut oil or of fresh fat with 40 parts of a 15 per cent solution of caustic potassa, mixing intimately with 30 parts of glycerin and heating carefully. This makes a yellowish, smooth and soft base.

Sapo unguinosus or sapo leniens is prepared by converting 100 parts of pure potassium carbonate into caustic potash, with 60–80 parts of quicklime, the solution being concentrated to sp. gr. 1.180; 400 parts of lard are added, the mixture stirred for half an hour, 40 parts of alcohol added, and the whole digested 12 hours in a covered vessel at 50°–60° C.; then 150 parts of glycerin added.

These bases are suited as vehicles for organic bodies, as balsam of Peru, phenols, sulphur, etc., but are incompatible with metallic salts, oxides and acids.

A mixture of doegling oil with wax has been proposed. This oil does not easily become rancid, and is readily absorbed by the skin. In order to make such a base miscible with aqueous fluids, soap may also be incorporated.

Under the name of "**myronin**," such a base is prepared by mixing sufficient carnauba wax with doegling oil to give an ointment-like consistence; then incorporating 10 or 20 per cent of stearine soap (stearate of potassium).

Unguentum Caseini.—Dr. Unna, the originator of this ointment-base, gives the following directions for its preparation: Take milk from which the cream or fat has been entirely removed, and curdle it by the addition of rennet at a temperature of 30° to 40° C. Assemble the coagulum and wash with running water until the washings no longer show an acid reaction; dry carefully and reduce to powder. Dissolve 34.5 parts of caustic potassa and 8.5 parts of caustic soda in 5,000 parts of water, and dissolve 1,400 parts of the casein in this solution. Now add 700 parts of glycerin and 50 parts of phenol, and, when these are dissolved, incorporate 2,100 parts of petrolatum and 50 parts of zinc oxide, and finally add enough water to make 10,000 parts. Thus prepared, casein ointment presents a perfectly homogeneous, semi-liquid, durable emulsion, which is, in fact, a sort

of thick and artificial milk, the petrolatum being in a condition of the minutest subdivision. It forms a soft and pliable film upon the skin, and is free from greasiness. Acids and acid salts are incompatible with it, coagulating the casein and causing separation of the base; but medicaments with only a slightly acid reaction which can be emulsionized, as tar, balsams, etc., can be incorporated to the extent of 20 per cent. Alkalis and alkaline salts, ichthyol, etc., thicken the base and the addition of more water becomes necessary. Metallic mercury can be incorporated to the extent of 33 per cent. Powdered substances may be first rubbed up with a little vaselin and then incorporated with the base.

The following table, prepared by A. St. Onge, shows the relative absorptivity of the different bases when manipulated in the usual manner. The figures are not absolute, but show the results of a series of carefully conducted experiments, and may be relied upon for guidance at the prescription counter:

100 PARTS OF BASE	AMOUNT OF WATER	AMOUNT OF ALCOHOL	AMOUNT OF GLYCERIN
Lard.....	15	9.05	100
Benzoinated Lard, U. S. P.....	17	8.36	100
Lard with Tr. Benzoin.....	17		
Lard with 1 per cent Benzoic Acid.....	12	6.22	80
Lard with Balsam Tolu.....	17		
Lard with Balm Gilead.....	17		
Lard with 5 per cent Glycerin.....	10	9.85	95
Lard with 2 per cent Resin.....	22	10.80	75
Lard with 10 per cent Petrolatum.....	4	4	50
Ointment.....	40	11.49	200
Cerate.....	40	13.25	100
Spermaceti Cerate.....	30	9.69	80
Cold Cream.....	50	5.68	300
Cocoonut Oil.....	100	54.8	50
Goose Oil (6) with Cacao Butter (1).....	30	47.94	200
Goose Oil (6) with Yellow Wax (1).....	100	37.67	600
Petrolatum.....	10	5.72	100
with 5 per cent Yellow Wax.....	40		
Cosmolin.....	15	8.54	100
with 5 per cent Yellow Wax.....	55		
Lucillin.....	12	6.09	100
with 5 per cent Yellow Wax.....	35		
Vaselin.....	12	11.14	100
with 5 per cent Yellow Wax.....	65		
White Vaselin.....	10	9.44	150
with 5 per cent White Wax.....	60		
Albolin.....	2	2.82	25
with 5 per cent White Wax.....	15		
Mollosin.....	112	14.50	100
Lanolin.....	200	8.14	200
Agnin.....	200	200	100
Anhydrous Wool-fat.....	300	7.5	300
Lanolin Ointment.....	150	8.86	200
Unguentum Lanolin.....	300	9.40	300
Adipatum.....	400	11.88	400
Epidermin.....	Indefinite	50	Indefinite
Mollin.....	Alm Indefinite	5.36	"
Casein Ointment.....	Indefinite	10 fluid, 25 breaks emulsion	"

OLEATES AND STEARATES

The oleates are often employed in ointments in preference to powdered chemicals, as they are more readily absorbed. Professor Hallberg states that they penetrate into, but not through, the skin. Some of these are adapted to extemporaneous preparation, and merit mention here. They are soluble in fats and oils, hence are more easily incorporated, and they often avoid the incompatibilities of water-soluble salts.

The true oleates are salts prepared with oleic acid, but all of the official oleates contain an excess of oleic acid, being prepared by dissolving the alkaloid or metallic oxide in the acid.

This is the method always chosen for making oleates of the alkaloids, and but little time is required. Oleic acid varies much in quality as found in the market, and it is desirable that only the purest should be used in preparing these, to avoid irritating qualities.

A light-colored acid is selected by preference, but purity and freedom from rancidity should be the prime requisites.

The free alkaloids (not the salts) are readily soluble in this. Solution is hastened by heat, but the oleate so made does not keep as well. The usual strength is 2 per cent of alkaloid, except morphine and cocaine, 5 per cent and quinine 25 per cent.

None keep well, and they should be made fresh.

The metallic oleates may be prepared in the same manner by dissolving the oxide in the acid. Heat and moisture favor the solubility, but hasten decomposition.

It is preferable to make these by double decomposition with a special prepared sodium or potassium oleate. On adding a soluble metallic salt to this, the corresponding oleate is precipitated as a soft unctuous mass, which is then washed and dried. These keep much better than when an excess of acid is present, and may be diluted to any strength desired.

If made with stearic acid instead of oleic, a fine powder is obtained instead of an unctuous mass.

Castile soap is sometimes used in place of sodium oleate, and an oleopalmitate is precipitated instead of a pure oleate.

Such are firmer than the true oleates, and may be stiff and plaster-like, as lead plaster, or pulverulent, as the commercial "oleate of zinc," so-called. Both of these may be made in this way.

PREPARATION OF OINTMENTS

Ointments are prepared by two general methods—mechanical mixing of the ingredients, or by fusion.

The first method is used when soft fats are mixed with insoluble bodies, the second method when waxes, resins, etc., are to be mixed with soft fats, or when medicinal ingredients are to be incorporated which are soluble in the warm fats; also to facilitate mechanical mixing.

The essential principle in ointment-making is to *start right, and go slow*, particularly at first. Powders, liquids etc. can be incorporated well if handled right, but impatience or haste will spoil ointments more often than ignorance or lack of skill.

Mechanical incorporation may be performed by trituration in a mortar, or on a glass slab by means of a broad and stiff spatula. The latter method is generally the better, except when a considerable amount of liquid is incorporated. It has this advantage, that lumpy particles are more easily pressed out. Ointments are also more easily and thoroughly transferred from a slab than from a mortar and pestle. A glass slab is to be preferred, because it is non-absorptive and readily cleansed. Two of these are convenient, the under sides being painted respectively black and white, then light-colored ointments are made over the dark background, and dark-colored ointments over the light, the condition of the mixtures being in this way easily watched. A steel spatula or putty-knife may be used in most cases when water is not present, since reactions of salts do not occur readily through the medium of fats.

It should not be used with citrine ointment, however, as this contains some nitric acid, nor with other mercury salts, tannin, etc., when water is present.

Mortars are preferred when much liquid is to be incorporated, or sometimes when a very hard ointment or cerate is to be mixed with a soft one. In such cases the hard or stiff ointment should be first trituated with a small quantity (one-half to an equal bulk) of the soft body until thoroughly admixed, then the remainder is added and incorporated. During the first mixing the hard fats will become somewhat softened by the trituration and the mixing is easier. If this is not done, lumps are formed in the mixture which are difficult to eradicate.

The same method should be followed when the mixing is performed on a slab.

Heat aids the mixing or incorporation very considerably, whether a mortar or a slab be used, by softening the fats and rendering the work easier. It also favors the solubility of bodies which are soluble in fats and oils. Many think that the incorporation of insoluble substances with melted fats makes a superior ointment, as well as being easier.

Relatively large quantities of liquids are best incorporated by adding them gradually to the fatty base, with constant trituration, as in making emulsions, or by first melting the fats and stirring in the fluid as the base cools. Such ointments are usually white and creamy, and more prone to spoil.

Glycerin and oils mix more readily in a warm mortar.

Extracts should always be softened before adding to fats or oils; aqueous extracts with water and alcoholic extracts with diluted alcohol. Alcohol is less readily incorporated than water.

Certain fluid and semi-fluid bodies, as balsam of Peru, storax, tar, ichthyol, etc., are difficult to incorporate with fats, and they separate in a granular form on standing. These are sometimes ordered in relatively large proportions. They mix better with castor oil than with most fats, and the use of castor oil with these is recommended. An equal or double amount is usually sufficient; being allowed for in the base directed. Another method of incorporation is by emulsifying them first with half their weight of yolk of egg. But yolk of egg must not be used with phenol, resorcinol, or other substances that coagulate albumin.

Petroxolin is the best base, pharmaceutically considered, for Peru balsam. This is a better solvent for the balsam than fats, and makes a smoother and more permanent ointment. It also combines well with storax, ichthyol etc.

Regarding the incorporation of liquids with ointments, Mr. A. St. Onge makes the following statement:

"Water when mixed with a base gives it a white and creamy appearance; alcohol does not whiten the base nor change the color, and glycerin makes a mass more or less translucent.

"The length of time taken to incorporate the base with the liquid must necessarily vary. When the proportion of liquid is small compared with the base, as in the case of lard and petroleum jellies, a minute or two is sufficient for complete saturation; bases that absorb from 35 to 65 parts of liquids can be saturated within 15 to 20 minutes, while wool-fat cannot be saturated within a reasonable time; it is not due so much to excessive amount of certain liquids that it will take as to its ropiness and stickiness, and its large increase in bulk when saturated. Fats diminish the stickiness of wool-fat and also its tendency to enormously increase in volume when incorporated with water.

"Bases saturated with water will not take glycerin and *vice versa*; water and glycerin can be used, however, in the same base. A base saturated with alcohol will take up water without the breaking of the mixture.

"**When two or more liquids** are to be incorporated into a base, their previous admixture seems to work better than the separate incorporation. Saturated bases with liquids are not permanent mixtures, the water and alcohol evaporating upon exposure, while glycerin has a tendency to separate upon standing; the glycerin appearing as fine globules all through the mass, and the mass becoming readily homogeneous upon stirring. Fats mixed with liquids within two-thirds of the saturating point are comparatively stable.

"Ointment bases containing white or yellow wax and the white paraffin jellies when saturated with water, will grow darker upon standing."

Powders which are insoluble in the fats or only slightly soluble in water must be first thoroughly incorporated with about an equal bulk of the base before the remainder is added. If in large proportion this is best accomplished in a warm mortar, even warm enough to melt the fat, and the trituration must be continued until the two are well mixed and no lumpy or gritty particles can be discovered. The remainder of the fat can now be very easily incorporated either as a liquid or a solid, and a smooth ointment results.

The mortar is easily heated by filling with hot water and allowing to stand a few minutes, or by burning half a drachm or so of alcohol in it.

Gritty ointments are an abomination to pharmacy, and are often mischievous when applied to a sensitive and sore surface. A pharmacist should never allow an ointment to leave a dispensing counter until it is perfectly smooth and homogeneous, when it may be soothing instead of irritating. This is not always easily accomplished, or rather quickly accomplished, sometimes requiring patience and plenty of muscle, but it is always worth the while.

There are now in the market mixtures of zinc oxide with oil made by grinding the two together in a paint-mill, thereby insuring a perfectly smooth though stiff paste. These may be used in place of the dry powder, but in making small quantities but little time will be saved by their use and the resulting ointment will be softer.

In some of the mercurial ointments, the salt is first rubbed to a fine powder with a little oil, partly for the above reason, and partly because these are liable to be reduced by friction if an attempt is made to powder them finely while dry.

Crystalline salts must first be rubbed to a very fine powder, or in case they are very soluble, as potassium iodide, etc., dissolved in a little hot water, except in case of eye-salves, when any risk of minute

crystals, which are liable to form in the hot solution before it can be thoroughly diffused, must be avoided. Minute and sharp crystals are exceedingly irritating and special pains should be taken to avoid them.

When water is inadmissible for this or other reasons, a few drops of oil may be employed. Eye-salves containing crystalline alkaloids are particularly troublesome in this regard. Water should be used only after careful consideration of the solubility for dissolving the crystals. The oleates of the

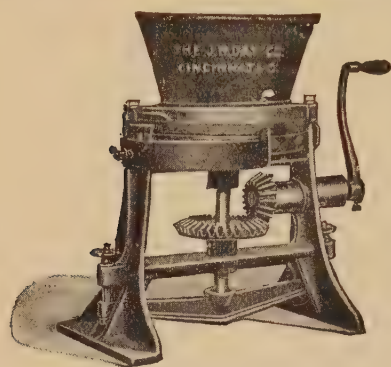


FIG. 63.—Ointment mill.

alkaloids are better when permitted by the physician, but care should be taken that these are fresh and free from rancidity. In lieu of these the salts should be triturated thoroughly with a little oil or a portion of the base, until rubbed to an impalpable powder.

For moderately large quantities of ointments, and particularly for such as contain gritty ingredients, **an ointment mill** is a practical necessity. The mill is always used on the manufacturing scale, and even for the small dispenser it often saves time as well as produces smoother ointments. Mills are obtainable for either hand or electric-motor power. The writer is reminded of one pharmacist who had a prescription calling for an ointment composed of potassium chlorate, Venice turpentine and lard—a particularly troublesome and difficult mixture—which he made by means of an ointment mill and so pleased the doctor that a considerable business resulted from it.

In preparing large quantities of ointments containing insoluble powders in large proportion, it is often more expeditious to partially incorporate the powder with the melted base, then rub the hot mixture through cloth, taking care that all the powder goes through with the fat. The strained mass should then be well stirred while cooling.

This plan of rubbing a soft ointment through a cloth works well with lumpy substances in small quantities, and may save much time.

Preparation by Fusion.—When wax, stearin, rosin, or other hard fusible bodies are to be incorporated with soft fats, it is necessary to melt both these and the soft fats to get a smooth, homogeneous mix-

ture. Such mixtures have a melting-point intermediate between those of its ingredients, and, if the quantities are equal, usually nearer to the lower point than the higher. The fusing-point cannot be calculated, but must be ascertained by experiment, if desired.

In mixing these bodies the invariable rule to be followed is to *melt the body having the highest fusing-point first, then add that having the next highest.*

Never place the cold ingredients together in a pan or capsule and try to melt all at once, because when this is done it is necessary to heat the entire mass to the fusing-point of the highest body before all will be melted, and more time and labor are required to secure a smooth fat from this hot liquid. When wax, spermaceti, and stearin are thus mixed with softer fats, it is necessary to stir the warm fluid while cooling to prevent congealing in a granular condition. Do not attempt to chill rapidly while doing this, or the hard fats and waxes are likely to separate, and require re-melting.

The operation is best performed by melting each body very slowly, then the fluid as first obtained will be near its congealing point and begin to solidify in a short time.

It is not necessary to continue stirring until the mixture is hard, but only until a pasty mass is obtained which is just stiff enough to prevent the separation or settling of the hard fats or insoluble powders. If continued beyond this, air is worked into the ointment, and it is more likely to spoil on keeping.

Resin and cacao butter do not have this tendency to separate, and stirring is therefore unnecessary.

It is possible to make wax-ointments also without stirring, but special care and watching are needed to see that the liquid does not get too hot, and little time or labor is saved. If the conditions are just right granulation will not occur, otherwise it will.

When bodies which are soluble in oils are to be incorporated in ointments and cerates, dissolving them in the melted base is often the best method.

Many such bodies are volatile or injured by heat, and an excess of heat should always be carefully avoided.

The heat is best applied by means of a water-bath, and the fat should not be melted too quickly. If the fat is not perfectly clear it should be strained before adding the medicinal agent.

When more of the soluble body is to be incorporated than will dissolve in the base, it is preferable to incorporate the whole mechanically.

Chemical changes occur not very frequently in the making of ointments and cerates.

In ointment of nitrate of mercury, elaidin is formed by the action of nitric acid upon lard, and mercury nitrate by the union of mercury and nitric acid. This is not within the bounds of extemporaneous pharmacy and a full discussion is out of place here. The official process will give satisfactory results if carefully followed, provided the nitric acid is of *full strength*.

In Goulard's cerate, a reaction takes place between the subacetate of lead and the fats in the camphor cerate, lead soap or plaster being formed. This will not keep well, and should be made fresh each time.

In iodine ointments the iodine partially combines with the fat, and all is not free. If sufficient unsaturated fatty acids or hydrocarbons are present, the so-called "stainless" iodine ointment is obtained.

STORING AND DISPENSING

Comparatively few of the ointments are permanent preparations. Those made of lard or suet tend to become rancid in a short time, and those made with petrolatum separate easily if stored in a slightly warm place.

Many of them change in color by action of light; citrine, chrysarobin, mercurous iodide, iodoform ointments and many others becoming dark, while iodine ointment first darkens, then becomes lighter. Ointments containing extracts of Peru balsam, tar and others separate on standing even if kept cold. Some metallic salts are reduced and some are oxidized, on standing in contact with fats, particularly if water is present.

Cerates are more permanent as a class, but some of these spoil quickly, notably Goulard's cerate.

All such should be made fresh as called for, or only in such quantities as will be quickly disposed of.

Ointments and cerates should always be stored in the coolest and driest available place. If kept in a warm place, the softening of the base is likely to cause a partial separation of the ointment; heat and moisture also favor chemical changes. When dispensed the patient also should be directed, either by labelling the box to that effect or verbally, to keep it in a cool place.

The best containers are those of amber or opaque glass, both for storing and dispensing. Earthen-ware containers are usually somewhat porous, and if a rancid ointment be once stored in them, they are not easily purified.

Pots with rounded inside surfaces, no sharp corners, are most convenient for removing the ointment for use, and they are also more easily cleaned.

Never mix a new ointment with the remains of an old lot, particularly when made of a vehicle liable to become rancid. The old ointment should be thoroughly removed from the pot before any of the new is inserted. The cleaning can be easily accomplished by rubbing with pine or other soft-wood sawdust, or with soft paper, then washing with caustic potash or ammonia-soap solution. This method is also useful for cleaning utensils with which ointments have been made.

Rather than take the trouble to clean the container each time an ointment is renewed, some prefer to use the cheaper chip boxes made of successive layers of wood veneer.

These are almost impervious, and are cheap enough so that a new box may be dispensed each time. The turned-wood boxes are practically worthless, as the fat quickly permeates the wood, and they become very disagreeable to handle.

In labelling the boxes the number of the prescription should be placed both on the top and bottom, so that if one label becomes obliterated or lost, the other will suffice for renewal.

Very soft ointments may be daintily dispensed in **collapsible tubes** such as are used for glycerin jellies, etc. Avoid putting a hard or stiff ointment into such.

The easiest way to fill a collapsible tube is to roll the ointment into a tube of stiff paper, insert one end of this into the open end of the collapsible tube, then draw the paper through the fingers so as to squeeze out the ointment and leave it in the tube.

Cerates are sometimes ordered to be spread like a plaster, particularly cantharides cerate. A little heat, sufficient to soften, but not melt the cerate, is admissible in such cases, but *hot* tools should not be used.

Contact with metal has been found to promote rancidity, hence metal containers are not advisable for storing ointments containing lard or other animal or vegetable fats. This objection also applies to collapsible tubes for dispensing, but may be of little consequence when the ointment is used up quickly. The use of metal boxes for dispensing ointments is more objectionable for this and other reasons.

PLASTERS

The making and spreading of plasters is a much less frequent operation now than it was before the era of the rubber and porous plasters. Plaster-making was once an important part of pharmacy, requiring skill, to acquire which much practice was necessary. At the present time the art is restricted mostly to the preparation and spreading of blistering plasters, and even these are not very frequent. Plasters are still largely used, but the demand is supplied almost entirely by manufacturers who use a rubber and resin basis.

The bases of official plasters are medicinally more active than those of ointments and cerates.

Lead plaster, which is essentially lead soap, is one of the most common. This has a sedative and mildly astringent action. Mixed with soap its action is still milder.

Resin and pitch have a stimulating action and impart adhesiveness.

Wax is used merely to impart firmness and is not often employed.

Gum resins and oleoresins are stimulating and also impart adhesiveness.

The purpose of plasters is two-fold: to afford protection and mechanical support, and to produce medicinal effects by slow absorption.

For the first reason plasters are always hard and possess little adhesiveness when cold. For convenience of handling they are made into the form of sticks or rolls, which may be protected from the air by wrapping in oiled or paraffined paper.

In only a very few cases are plasters soft enough to be handled conveniently in mass.

Plasters with fatty or soap bases should never be kept already spread, as they become brittle and discolored.

Preparation of Plasters.—Plasters are always made by fusion or solution.

By fusion the process is very similar to the making of cerates, etc.

The body having the highest melting-point is fused first, then the others are added in order and lastly the medicinal ingredients.

If straining is necessary it should be done before the medicinal matter is added. When these are soluble in the plaster ingredients the mass is kept fluid, at as low a temperature as possible, until the medicinal matter is all dissolved, and thoroughly mixed with the base. Alcoholic extracts are better adapted for plasters than aqueous, for this reason. If the extracts are injured by heat they should be diffused or incorporated as quickly as possible, but with the least heat.



FIG. 64.—Plaster iron.

Volatile bodies, as menthol, camphor, etc., are to be treated in the same way.

Insoluble powders, etc., are stirred into the mass while cooling.

The mass should be rolled into sticks while still warm. This is easily done on a glass or porcelain slab by rolling with the hands, or with a flat stick of wood. If the mass contains much resin or pitch, a little petrolatum will prevent its sticking to the hands and utensils. Lead plaster does not need this. This should be kneaded thoroughly before rolling to work out the excess of water. If left in the mass the plaster appears whiter, but it oxidizes more quickly and does not make as nice a mass when mixed with other bases.

Resinous plasters may sometimes be whitened by pulling and kneading, air being worked into them in this way.

The sticks can be made of any convenient size, usually of a size to fit the can or bottle in which they are to be stored.

Spreading.—Plasters are spread upon skin, silk, cotton cloth or paper.

The large plasters are best spread upon sheep or chamois skin, but cotton cloth will serve nearly as well if the customer does not care to pay for the skin. Small plasters are spread upon thin cloth or brown paper, sometimes upon flexible adhesive plaster, which is sold for this purpose by plaster manufacturers.

The design is first marked upon a piece of cardboard and then cut out, making a stencil form, which is placed over the skin or cloth and filled in with the plaster. The form should have a wide margin, and by preference should be of the same thickness as the desired plaster. It may be tacked upon the cloth, or, if first dipped into water, it will adhere fairly well in the moist condition and will not interfere with the spreading.

Forms are kept, of tinned iron or sheet zinc, in some cases. These are very useful for ear plasters, but the others are likely to vary in size, as ordered. It will be found easier to cut or trim the cloth upon which the plaster is placed after spreading.

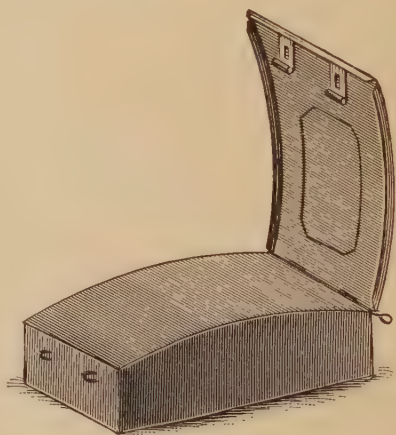


FIG. 65.—Plaster form.

The plaster is melted in a convenient dish, poured upon the cloth while hot, and spread over its surface with a few rapid strokes of a large spatula or plaster-iron, previously heated. Plasters which have been spread slowly usually have a crinkly or striped surface. They are much more apt to be smooth and of an even thickness if spread rapidly.

The plaster should not be hot enough to soak through the skin or cloth and stain the under side, and the spreading spatula should be only warm enough to obviate congealing the soft mass. Plaster-irons may be obtained which will retain their heat for a long time or which are self-heating.

Hollow rollers are also used which may be filled with hot water, and are useful for giving a smooth finish, but are not good for spreading.

Cantharides cerate should be spread with a warm spatula or iron, but without melting.

The cloth should not be trimmed close to the plaster; a margin of half an inch or so should be left all round.

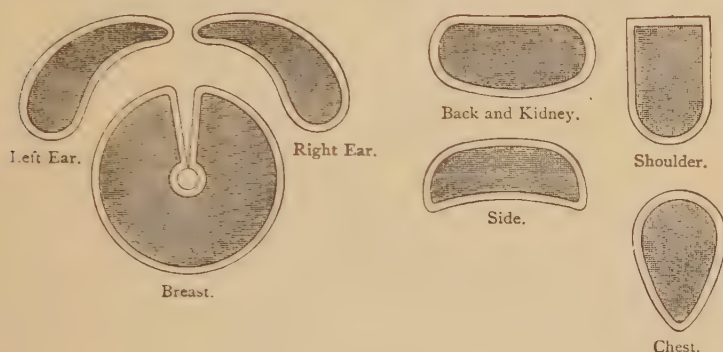


FIG. 66.

Ear-plasters may be trimmed close on the inner edge where it fits against the back of the ear, a margin being left on the remaining sides.

A sheet of tissue or oiled paper should be placed over the surface of the plaster before dispensing; then the plaster may be placed in a box or formed into a roll.

Rubber plasters are essentially an American industry of comparatively recent date. The basis of these is a mixture of best Para rubber with olibanum (true frankincense), pitch, wax, etc., worked together entirely by mechanical means. Attempts were made in the early days of the industry to use solvents for incorporating these and obtaining a homogeneous mixture, but these failed, the rubber never being itself again after solution.

The rubber is first soaked and steamed; then passed through spirally corrugated iron rolls, under a stream of water, until well cleansed.

This forces it out in crinkled sheets, which are hung up to dry and season. The freshly exposed surfaces are a very light brownish-yellow at first, but exposure to the air soon turns them dark and even black.

The sheets are then worked on warm, smooth calender mills to a perfectly homogeneous mass.

The olibanum, or frankincense, to which the fragrant odor of these plasters is mostly due, is stamped and sifted, while the pitch and wax are purified by melting and straining.

The ingredients are then mixed by working on the warm calender mills, and the medicinal ingredients are incorporated in the same way. The mass is spread, while still warm and plastic, by means of heavy calenders. The cloth, measuring usually 120 yards by 36 inches, is fed through the calenders, and passing under the lower roll, is connected with a large reel behind the machine. The calenders being gauged for the right thickness are started and the mass fed upon the cloth, between guides.

After standing for a time upon the reels, to cool and harden, the plaster is wound upon wooden drums, cut into strips the width of the finished plaster, and these are afterward cut transversely and perforated. About 100,000 plasters may be spread per day on one machine.

These plasters are very flexible, and adhere well to the skin, the medicinal qualities being readily absorbed. When of the best quality, they retain their flexibility for a long time; but some grades will become brittle and non-adhesive after a time.

These can be temporarily restored by warming and wetting with spirit of camphor, or with a bland oil.

The rubber being the most expensive ingredient, attempts have been made to find a substitute for it; but the flexible and adhesive qualities cannot be satisfactorily secured without this. Among the materials suggested are chicle, vulcanized oil, varieties of asphaltum, and a base consisting of glue, glycerin, and an alkaline sulphoricinoleate.

OINTMENTS, CERATES AND PLASTERS

I

- R. Ammoniated mercury, in
 very fine powder..... 10 Gm.
 Liquid petrolatum..... 10 Gm.
 Hydrous wool fat..... 40 Gm.
 White petrolatum..... 40 Gm.
 M. Sig.—White precipitate ointment.
- Rub the ammoniated mercury with the liquid petrolatum until smooth, then add the petrolatum and wool fat previously melted and stir until it congeals.
 Make 20 Gm.

2

- R. Red mercuric oxide, in
 very fine powder..... 10 Gm.
 Distilled water..... 10 Gm.
 Lanolin, anhydrous..... 40 Gm.
 Petrolatum..... 40 Gm.
 M. Sig.—Red precipitate ointment.
- Triturate the red mercuric oxide with the water, then with the lanolin, until smooth, then gradually incorporate the petrolatum and mix thoroughly.
 Make 20 Gm.

3

- R. Yellow mercuric oxide in
 very fine powder..... 1 Gm.
 Liquid petrolatum..... 1 Gm.
 Hydrous wool fat..... 10 Gm.
 Petrolatum..... 88 Gm.
 M. Sig.—Ointment of yellow mercuric oxide.
- Triturate the yellow mercuric oxide with the liquid petrolatum until it is perfectly smooth, add the hydrous wool fat, and finally incorporate the petrolatum. Avoid contact with metallic implements.

- 4
 R. Potassium iodide..... 10 Gm.
 Sodium thiosulphate..... 1 Gm.
 Water, hot..... 10 cc.
 Benzoinated lard..... 80 Gm.
 M. Sig.—Potassium iodide ointment.
- 5
 R. Iodine..... 4 Gm.
 Potassium iodide..... 4 Gm.
 Glycerin..... 12 Gm.
 Wool fat..... 80 Gm.
 M. Sig.—Iodine ointment.
- 6
 R. Iodine..... 5 Gm.
 Paraffin..... 5 Gm.
 Oleic acid..... 20 Gm.
 Petrolatum..... 70 Gm.
 Sig.—Stainless iodine ointment.
- 7
 R. Extract of stramonium... 10 Gm.
 Diluted alcohol..... 5 cc.
 Hydrous wool fat..... 20 Gm.
 Benzoinated lard..... 65 Gm.
 M. Sig.—Stramonium ointment.
- 8
 R. Lead plaster..... 50 Gm.
 White petrolatum..... 49 Gm.
 Oil of lavender..... 1 Gm.
 M. Sig.—Diachylon ointment.
- 9
 R. Sublimed sulphur..... 15 Gm.
 Benzoinated lard..... 85 Gm.
 M. Sig.—Sulphur ointment.
- 10
 R. Zinc oxide..... 20 Gm.
 Paraffin..... 15 Gm.
 White petrolatum..... 65 Gm.
 M. Sig.—Zinc oxide ointment.
- 11
 R. Zinc oleate..... 50 Gm.
 Petrolatum..... 50 Gm.
 M. Sig.—Zinc oleate ointment.
- 12
 R. Mercury..... 50 Gm.
 Mercuric oleate..... 2 Gm.
 Suet..... 23 Gm.
 Benzoinated lard..... 25 Gm.
 Sig.—Stronger mercury ointment.
- "Dissolve the potassium iodide and the sodium thiosulphate in the hot water, then mix the solution with the benzoinated lard."
 Make 20 Gm.
- "Rub the iodine and the iodide of potassium, first with the glycerin, and then with the wool fat, gradually added, until they are thoroughly mixed, avoiding the use of metallic utensils."
 Make 20 Gm.
- Dissolve the iodine in the oleic acid by heating to about 65–70° C. add the paraffin and continue the heat until the liquid no longer has a reddish color; then add the petrolatum, and when all is liquefied remove from the heat and stir frequently until it congeals.
- "Rub the extract with the diluted alcohol until it is uniformly soft; then gradually add the lanolin, then the benzoinated lard, and mix thoroughly."
 Make 20 Gm.
- "Melt together the lead plaster and white petrolatum, on a water-bath; then add the oil of lavender, remove from the heat and stir until the ointment congeals."
 Make 25 Gm.
- Rub the sulphur with the lard gradually added until they are thoroughly mixed.
- Rub the zinc oxide with an equal weight of the melted paraffin and white petrolatum until smooth, then incorporate the rest of the base.
- Heat them together on a water-bath until the oleate is dissolved in the melted petrolatum, then remove from the heat and stir until it congeals.
- Triturate the mercury with the mercuric oleate until the mercury is emulsified. Melt the suet, add the lard, and allow the mixture to partially cool. Add about 3 Gm. to the mercury mixture, and triturate until the globules of mercury are no longer visible, then gradually add the remainder of the fats and continue the trituration until the ointment has become of a deep bluish color.

13

- R. Spermaceti..... 125 Gm.
 White wax..... 120 Gm.
 Expressed oil of almond. 560 Gm.
 Stronger rose water..... 190 cc.
 Sodium borate, in fine
 powder..... 5 Gm.
 M. Sig.—Cold cream.

"Reduce the spermaceti and the white wax to fine shavings, and melt them at a moderate heat. Then add the expressed oil of almond, pour the mixture into a warmed, shallow Wedgwood mortar, carefully add, without stirring, the whole of the stronger rose water in which the sodium borate had previously been dissolved by a gentle heat, and stir rapidly and continuously, until the mixture becomes uniformly soft and creamy." Make one-twentieth the above quantities. Do not stir too long.

14

- R. Cerae albæ..... 14.0 Gm.
 Adipis lanæ..... 3.5 Gm.
 Petrolati liquidi..... 55.0 Gm.
 Aquæ rosæ..... 27.5 Gm.
 M. Sig.—Toilet cold cream.

Melt the wax, add the lanolin, then the liquid petrolatum, and lastly add the rose water and stir until it congeals.

15

- R. Cerae albæ..... 16.2 Gm.
 Petrolati liquidi..... 58.0 Gm.
 Sodii boratis..... 0.8 Gm.
 Aquæ rosæ..... 25.0 Gm.
 M. Sig.—Permanent cold cream.

Melt the wax, add the liquid petrolatum, then stir in the rose water previously warmed and containing the borax. Stir until the whole congeals.

16

- R. Adipis..... 3 viij
 Cerae flavæ..... 3 ss
 Cetacei..... 3 ss
 Sodii boratis..... 3 ijss
 Cucumeri..... ij no.
 M. Sig.—Cucumber cream.

Melt together the lard, wax and spermaceti and stir while cooling. Peel and slice three (fair-sized) cucumbers, and mix with the ointment, with which half the borax has been incorporated. Allow to stand 10 hours, then melt, strain, chill on ice and separate the watery layer, and incorporate the remainder of the borax.

17

- R. Resin cerate..... 650 Gm.
 Oil of turpentine..... 350 Gm.
 M. Sig.—Turpentine liniment.

"Melt the resin cerate in a capsule, on a water-bath, then add the oil of turpentine, and mix them thoroughly." Make 20 Grams.

18

- R. Zinci oxidi..... 1.0
 Camphoræ..... 0.150
 Unguenti..... 20.0
 M. Ft. ungt. Sig.—Eye salve.

Melt half the ointment and dissolve the camphor in the warm fat, incorporate the zinc oxide, then the remainder of the ointment.

19

- R. Cocainæ hydrochloridi..... gr. v
 Petrolati..... 3 j
 M. Sig.—Apply to the eyes.

20

- R. Ung. hydrargyri,
 Ung. aquæ rosæ..... aa 10.0

21

- R. Hydrarg. chlorid. corros... Gr. ij
 Petrolati..... 3 j
 M. Ft. ung.

Dissolve the corrosive sublimate in 30 minims of alcohol, mix this with a drachm of castor oil, then incorporate 7 drachms of petrolatum, avoiding contact with a steel spatula.

- 22
 R. Thymol..... 3 j Melt the lard, dissolve the thymol
 Adipis benz 3 j therein, and stir while cooling.
 M. Ft. ungt.
- 23
 R. Ung. hydrarg. nit., Work cautiously, and avoid the use of
 Ung. aquæ rosæ.....aa 10.0 metallic implements.
 M.
- 24
 R. Camphoræ, Triturate the chloral and camphor
 Chloralis hyd.....aa 4 together in a mortar until completely
 Petrolati..... 15 liquefied, and add the petrolatum.
 M. Ft. ung. Sig.—Ad partem dolen-
 tem applicetur.
- 25
 R. Ext. eucalypti, Soften the extracts with glycerin, and
 Ext. hydrastis, mix with the petrolatum. Water or
 Ext. irid. versic.....aa 3 j alcohol, if used for softening, does not
 Petrolati..... 3 j mix well with the petrolatum.
 M. Ft. ung.
- 26
 R. Ext. phytolaccæ bac. fld.... 3 j Melt the lard, add the fluid extract
 Adipis 3 j and stir while cooling. A smooth oint-
 M. Ft. ung. ment results without previous evapora-
 tion of the fluid extract.
- 27
 R. Pulv. sodii boratis..... 3 ss Dissolve the borax in the glycerin by
 Calcii hyposulphit..... 3 j aid of heat, stir in the calcium hypo-
 Glycerini..... 3 j sulphite, previously powdered, then
 Petrolati..... 3 ij incorporate with petrolatum.
 M. Ft. ung.
- 28
 R. Naphtholi..... 2 Dissolve the naphthol in 3 cc. of
 Petrolati..... 20 ether and mix with 5 Gm. of petrolatum.
 M. Ft. ung. Warm on the water-bath until the ether
 is entirely expelled, stirring the while,
 then incorporate the remainder of the
 petrolatum. Aristol ointment may be
 made in the same way.
- 29
 R. Aristol..... 5.00 Rub the aristol to a smooth cream
 Petrolati..... 45.00 with an equal weight of almond oil, then
 M. Ft. ung. incorporate 40 Gm. of petrolatum,
 gradually added.
- 30
 R. Resorcin..... 3 ss Rub the resorcin and zinc chloride
 Zinci chloridi..... gr. x with half a drachm of alcohol, and
 Petrolati..... 3 j incorporate the petrolatum.
 M. Ft. ung.
- 31
 R. Acid salicylic..... 3 ij Dissolve the salicylic acid in a little
 Menthol..... 3 ss ether, mix with the petrolatum and
 Olei gaultheriæ..... 3 ij warm gently until the ether has evap-
 Adipis lanæ..... 3 iv orated. Mix the oil in which the
 Petrolati..... 3 iv menthol has been dissolved with the
 lanolin, then mix with the petrolatum
 mixture.
 M. Ft. ung.

- 32
- R. Phenoli..... 1.0
 Unguenti..... 19.0
 M. Ft. ung.
- 33
- R. Olei amygdalæ expres..... 4
 Cetacei..... 8
 Ceræ albæ..... 4
 Camphoræ..... 1
 M. Sig.—“Camphor ice.”
- 34
- R. Adipis lanæ hydros..... 5.0
 Sulphuris præcip..... 5.0
 Zinci oxidi..... 2.5
 Ol. amygdal. express..... 5.0
 M. Ft. ung. Sig.—Toilet unguent.
- 35
- R. Yellow mercuric oxide, in
 fine powder..... 25 Gm.
 Oleic acid..... 75 Gm.
 M. Sig.—Oleate of mercury.
- 36
- R. Bals. Peruvian..... 3 iv
 Sulphuris..... 3 i
 Acidi salicylici..... 3 vi
 Petrolati albi..... 3 vi
 M. Ft. ung.
 Sig.—Apply as directed.
- 37
- R. Sulphuris præcip..... 3.0
 Resorcin..... 1.5
 Olei theobromat..... 12.0
 Olei amygdal exp..... 15.0
 Olei rosæ..... 0.2
 M. Ft. ung.
- 38
- R. Camphor liniment..... 100 Gm.
 White wax..... 350 Gm.
 White petrolatum..... 150 Gm.
 Lard..... 400 Gm.
 M. Sig.—Camphor cerate.
- 39
- R. Solution of lead subacetate 20 Gm.
 Wool fat..... 20 Gm.
 White wax..... 20 Gm.
 White petrolatum..... 38 Gm.
 Camphor..... 22 Gm.
 Mix
 M. Sig.—Goulard’s cerate.
- 32
- This is best made by dissolving the phenol in the warm ointment and stirring until cold.
- 33
- Mould in glass tubes.
- 34
- “Introduce the oleic acid into a suitable vessel and add to it the yellow mercuric oxide by sifting it upon the surface of the acid, and incorporate it by continuous stirring. Then set the mixture aside in a warm place, at a temperature not exceeding 50° C. (122° F.) and stir frequently, until the oxide is dissolved.”
 Make one-fiftieth the quantity. If heated too much the oleate becomes discolored and does not keep well.
- 36
- Mix the Peru balsam with 4 drachms of alcohol and incorporate with the white petrolatum. Then add the sulphur, then the salicylate. A smooth ointment is secured in this way. (Dunning.)
- 37
- Melt the cacao butter and add the almond oil. Dissolve the resorcin in a little water and mix with the sulphur, then with the oils, adding the rose oil. (Lascoff.)
- 38
- “Melt the white wax, white petrolatum and lard with the aid of a gentle heat; then add the camphor liniment, and stir the mixture occasionally, until it has become cold.”
 Make 20 Gm.
- 39
- Melt the white wax and white petrolatum, remove from the heat and dissolve the camphor in the mixture. Add the wool fat, incorporate thoroughly then gradually add the solution of lead subacetate and stir until smooth.
 Make 25 Gm.

- 40
 R. Resin..... 350 Gm.
 Yellow wax..... 150 Gm.
 Lard..... 500 Gm.
 M. Sig.—Basilicon ointment.
 “Melt them together at a moderate heat, strain the mixture through muslin and allow to cool without stirring.”
 Make one ounce.
- 41
 R. Chloretone..... 5 ss
 Mercurochrome gr. xx
 Ung aquæ rosæ..... 3 iii
 M. Ft. ung.
 Melt together 120 grains of spermaceti, 115 grains of white wax, and add 537.5 grains of expressed oil of almond, add the chloretone and continue the heat until all is dissolved. Dissolve the mercurochrome and 5 grains of borax in 192 minims of stronger rose water, heat to 65° C., add to the oil mixture and stir until it creams well.
- 42
 R. Bismuthi subnitratis..... 3 iv
 Olei ricini
 Glycerini.....aa 3ss
 M. Sig.—For external use.
 Mix the bismuth subnitrate first with the castor oil, then incorporate the glycerin. Makes a smooth ointment-like preparation.
- 43
 R. Acidi borici..... 3 iss
 Zinci oxidi
 Amyli
 Bismuthi subnit.....aa 3 i
 Olei olivæ..... 3 i
 Adipis lanæ..... 3 iii
 Liq. calcii hydrox..... 3 iii
 Aquæ rosæ..... 3 iss
 M. Ft. ung.
 Mix starch, olive oil, and rose water, add the lime water, then the lanolin and mix well. Mix the zinc oxide, bismuth subnitrate and boric acid, and gradually add the first mixture in a warm mortar.
- 44
 R. Iodi..... gr. xxiv
 Methylis salicylat..... 3 ii
 Adipis lanæ..... 3 iv
 Olei gossypii.....ad. 3 vi
 M.
 The iodine will dissolve in the warm oil, but will also combine with it and form a dark compound. The finished preparation will contain no free iodine.
- 45
 R. Resin, in fine powder... 140 Gm.
 Lead plaster..... 800 Gm.
 Yellow wax..... 60 Gm.
 M. Sig.—Adhesive plaster.
 “Melt the lead plaster and yellow wax together with a gentle heat; then add the resin, and, when it is melted, mix the mass thoroughly.”
 Make one ounce.
- 46
 R. Soap, dried and in coarse powder..... 10 Gm.
 Lead oleate plaster..... 90 Gm.
 Water, a sufficient quantity.
 M. Sig.—Soap plaster.
 “Rub the soap with enough water to reduce it to a semi-liquid state; then mix it with the lead plaster, previously melted, and evaporate to the proper consistence.”
 Make one-twentieth the quantity.
- 47
 R. Emplastri plumbi.... 2"×3"
- 48
 R. Emplastri cantharidis pro auribus..... No. ij
 Sig.—To go behind the ears.
- 49
 R. Camphoræ..... 22 Gm.
 Cere albæ..... 11 Gm.
 Adipis..... 67 Gm.
 M. Ft. ung. Sig.—Camphor ointment, N. F.
 Melt the white wax, add the lard, the camphor, and continue the heat until the camphor is dissolved, then stir until cold.

50

R.	Bismuthi subnitratis.....	3 ij	This is best made in a warm mortar with melted lard. A very stiff ointment results.
	Zinci oxidi.....	3 j	
	Acidi salicylici.....	gr. x	
	Amyli.....	3 ij	
	Adipis.....	5 vj	
M.	Ft. ung.	Sig.—Apply 2 or 3 times daily.	

Prescriptions from State Board Examinations

FOR CRITICISM AND PRACTICE

I			2		
R.	Ext. belladonnæ.....	gr. x	R.	Bismuthi subnit.....	3 i
	Acidi tannici.....	5 ss		Zinci oxidi.....	3 ss
	Zinci oxidi.....	3 ss		Amyli.....	3 i
	Ungt. petrolat.....	ad. 3 ss		Adipis.....	3 iii
M.	Ft. ung.	(Ind.)	M.	Ft. ung.	Sig.—Apply t. i. d.
3			4		
R.	Ung. hydrarg. oxid flav....	10.00	R.	Potass. iodidi.....	10.0
	Sig.—Ointment.			Potass. carbonat.....	0.6
	(How much yellow oxide of mercury,			Aquæ.....	10.0
	Troy weight, is required?) (Wash.)			Adipis benzoinat.....	80.0
			M.	Ft. ung.	Mitte 3 ss. (Pa.)
5			6		
R.	Sulphuris.....	3 i	R.	Bismuthi oxidi.....	2.0
	Phenol.....	3 ii		Acid oleici.....	2.0
	Ung. hydrarg. nit.....	3 iv		Ceræ albæ.....	4.0
	Ol. olivæ.....			Petrolati.....	8.0
	Ceræ flav.....	aa 3 ii		Misce ft. ung. sec. art.	
M.	Ft. ung.			Sig.—Ointment of bismuth oleate.	
	Sig.—Apply at night. (Minn.)			(Wash.)	
7			8		
R.	Sulphuris.....	3 i	R.	Hydrargyri,	
	Phenol.....	3 ii		Adipis lanæ.....	aa 3 ii
	Ung. hydrarg. nit.....	3 iv	M.	Ft. ung.	
	Ol. olivæ.....			Sig.—Apply as directed. (Wash.)	
	Ceræ flavæ.....	aa 5 ii			
M.	Ft. ung.				
	Sig.—Apply at night. (Wash.)				
9			10		
R.	Hydrarg. oxid flav.....	gr. ii	R.	Calaminæ præp.....	5.00
	Lanolini,			Petrolati.....	12.50
	Petrolati.....	aa q. s. ut. ft. 3 ii		Adipis benzoinat.....	12.50
M.	Ft. ung.	Sig.—Use on eyelids at night. (Ind.)	M.	Ft. ung.	(N. Y.)
11			12		
R.	Adipis lanæ.....	10.0	R.	Acid oleic.....	3 ii
	Acidi acetici dil.....	11.0		Atropinæ.....	gr. x
	Adipis benzoinat.....	10.0		Adipis.....	ad. 3 i
	Sulphuris præcip.....	3.0	M.	Ft. ung.	(Br. Col.)
M.	Ft. ung.	(Pa.)			
13			14		
R.	Ung. hydrarg. oxid rubri....	10.0	R.	Sulphuris loti.....	2.00
	Sig.—As directed. (Col. and N. Y.)			Potass. carb.....	1.00
				Aquæ.....	0.50
				Adipis benzoinat.....	15.00
			M.	Ft. ung.	(Vt.)

15

- R. Acidi gallici..... 0.5
 Ext. belladonnæ..... 1.5
 Alcohol dilut..... q. s
 Adipis lanæ..... 3.00
 Adipis benzoinat..... 9.75
 M. et ft. unguentum.
 Sig.—Apply twice daily. (Ill.)

17

- R. Potass. iodid..... 5 i
 Adipis lanæ..... 3 i
 M. Ft. ung.
 Sig.—Use externally. (Mass.)

18

- R. Plumbi acet..... ᠓ i
 Picis liquid..... 5 ss
 Pulv. opii..... 3 i
 Ung. paraff. alb..... 3 i
 M. Ft. ung.
 Sig.—Hora decub. indies utend.
 (Br. Col.)

20

- R. Emplast. cantharidis 3 × 4
 (Fresh spread.)
 Sig.—Apply as directed. (Ill.)

22

- R. Iodi resublim..... gr. x
 Adipis lanæ..... 3 ii
 Petrolati..... ad. 3 i
 M. Ft. ung. Sig.—Apply locally.
 (N. Y.)

24

- R. Mentholi 5 per cent
 Methylis salicylatis.. 8 per cent
 Adipis lanæ..... 15 Gm.
 M. Ft. inunctio. Sig.—Ut dictum.
 (N. Y.)

26

- R. Bismuthi subnit..... 3 ii
 Zinci oxid..... 3 i
 Acidi salicylici..... 3 ss
 Amyli..... 3 ii
 Petrolati..... 3 i
 M. Ft. ung. leve.
 Sig.—Apply locally. (Fla.)

28

- R. Acidi salicylici..... 3 ii
 Sulphuris..... 3 ii
 Bals. peruv..... 3 ii
 Phenol..... 3 i
 Petrolati..... ad. 3 ii
 M. Ft. ungt. Sig.—Apply locally.
 (Fla.)

16

- R. Sulphuris..... 3 ss
 Ammon. chlorid,
 Potass. carb..... aa gr. xx
 Adipis benz..... ad. 3 ss
 M. Ft. ung.
 Sig.—Apply as directed. (Ill.)

19

- R. Zinci oxid..... ᠓ ii
 Picis liq..... 3 i
 Betanaphthol..... gr. xv
 Paraff. moll..... 3 i
 M. Ft. ung.
 Sig.—More dicto partes affect.
 applic. (Br. Col.)

21

- R. Hydrarg. oxid flav..... gr. iv
 Atropinæ sulph..... 3 i
 Adipis lanæ..... gr. ii
 Petrolati..... ad. 3 i
 M. Ft. ung.—Sig.—Apply to eye at
 bedtime. (Fla.)

23

- R. Zinci oxidi..... 4.0
 Amyli..... 8.0
 Calaminæ..... 5.0
 Ung. aquæ rosæ..... ad. 30.0
 M. Sig.—Externally twice daily.
 (N. Y.)

25

- R. Hydrarg. ammon. alb..... 0.30
 Petrolati albi..... 10.00
 Misce exactissime ut fiat unguentum.
 Signa.—For the eyes. (Mo.)

27

- R. Ung. argenti nitratis, 2 per cent 3 v
 Sig.—Apply to affected area. (Fla.)

29

- R. Hydrarg. oxid flav..... gr. iv
 Atropinæ sulph..... gr. ii
 Adipis lanæ..... 3 i
 Petrolati..... ad. 3 i
 M. Ft. ung. Sig.—Apply to the
 eye at bedtime. (Ill, Fla.)

30

R.	Acidi salicylici.....	℥ ii
	Resorcinolis.....	℥ i
	Sulphuris.....	℥ ii
	Bals Peruv.....	℥ ii
	Adipis lanæ.....	℥ iv
	Petrolati.....ad.	℥ iii
M.	Ft. ung. (Fla.)	

32

R.	Glycerin.....	1.2
	Adipis.....	8.0
	Kali iodidi.....	0.4
	Iodi.....	0.4
M.	Ft. ung. Sig.—Admov et nocte. (Col.)	mane

31

R.	Potass. iodidi.....	5 per cent
	Aq. dest.....	q. s.
	Adipis benzoinat.....	20.0 Gm.
M.	Ft. ung. album.	
	Sig.—Applicandum omni nocte.	

33

R.	Hydrarg. oxid flav.....	gr. xv
	Petrolati albi.....	℥ i
	Adipis lanæ hyd.....	℥ i
	Aquæ.....	℥ xv
M.	Ft. ung. Sig.—Admove mane et nocte. (Col.)	b. i. d.

CHAPTER XIV

MISCELLANEOUS EXTERNAL PREPARATIONS

Poultice or Cataplasm (Lat. *Cataplasma, tis*).—A soft, mushy preparation, composed usually of some mealy substance capable of absorbing a large amount of liquid, made into a paste with hot liquids, and spread thickly upon cloths, then applied to the body while hot.

Fomentation (Lat. *Fomentum-i*).—A poultice composed of herbs or other non-absorptive material and hot liquids or lotions, absorbed in woolen cloths and applied hot.

Spongio-piline.—A thick cloth containing small pieces of sponge on one side and rubber or other water-proof material on the other, intended for the absorption and application to the skin of hot liquids.

Plaster Mull.—A thin cloth covered on one side with rubber or gutta-percha, or attached to gutta-percha tissue, upon which a medical agent in liquid form is spread or painted. These are used in the same way as plasters, absorption being facilitated by the impervious nature of the cloth.

Salve Mulls (Lat. *Steatina, æ*) or **Steatins**.—Ointments of high fusing-points containing dissolved medicinal agents, and spread upon gauze or mull in a manner similar to plaster mulls. The base is suet or lard with wax or lead plaster.

Plasmas (Lat. *Plasma, atis*).—Non-fatty, unctuous preparations, designed as substitutes for ointments, cerates, etc., in the local application of remedies, or as a substitute for poultices.

Caustics or Escharotics (Lat. *Escharotica, æ*).—Substances used for the destruction of tissues by the caustic action of chemicals or by heat. They are commonly used in the form of pastes or pencils.

Pastes (Lat. *Pasta, æ*).—Dermatologic applications of ointment-like consistency consisting largely of starch, flour, dextrin, chalk, or other

diluent with glycerin, soft soap, petrolatum or lard, etc., as a base.

Petroxolins (Lat. *Petroxolinum-i*).—Liquid or solid applications composed of soft soap and liquid or solid petrolatum, miscible with water and other fluids, and containing medicinal matters usually in solution.

Paints (Lat. *Litus, oris, or pigmenta, æ*).—Fluid or soft preparations applied with a camel's-hair brush. They are used in the forms of

(1) **Collodions** (Lat. *Collodium, i*).—Solutions of pyroxylin in ether-alcohol, with or without medicinal agents and which leave a hard film on drying.

(2) **Drying Liniments** (Lat. *Linimenta Exsiccantia, æ*).—Mucilages of gums or albumin, medicated, which leave a thicker but less tenacious film than the collodions on drying.

(3) **Glycero-gelatins** (Lat. *Gelatina, æ*).—Medicated globules of gelatin with glycerin, similar except in form and consistency to gelatin suppositories, which are melted at the time of use and applied with a brush.

Pencils or Crayons.—These are of two kinds—the **hard soluble pencils** (Lat. *Stilus dissolubilis* or *Stilus dilubilis* or *Stilus medicamenti*) composed of small sticks of moulded chemicals, used mostly as caustics or astringents, or of medicinal agents mixed with a stiff mucilage of tragacanth, starch or other gums, and formed into sticks which are then dried, and **Salve Pencils** (Lat. *Stilus unguenti*) mixtures of waxes, oils, resins, etc., with medicinal agents (astringent, antiseptic, cooling, etc.) and moulded into stick form. Camphor ice is a type of these.

Moxas.—Small cones of combustible matter, with an oxidizing agent, which glow, but do not inflame when ignited, and give out an intense heat; intended for cauterization by direct heat.

Poultices are seldom prepared by the apothecary, but he is frequently called upon for directions for preparing and applying them. They owe their virtues in part to the moist heat which they contain, and therefore need to be renewed every few minutes, except in the case of mustard poultice, which acts through the volatile oil formed therein. The other poultices may be used again and again, simply requiring to be re-heated each time before applying. They should be applied as hot as can be borne, and covered with thick cloths while upon the person, to prevent loss of heat. A good test of their temperature is their application to the back of the hand, which should be borne easily. The preparation of linseed poultice may be taken as a type of all these.

This is made by quickly stirring about 10 fluidounces of boiling water into 4 ounces of linseed meal, contained in a warm dish or pan. The mush thus made is then spread thickly upon a piece of cotton or linen cloth, and immediately applied to the skin. If the skin is first greased slightly with a little lard or oil, sticking will be prevented. When the poultice has become only lukewarm, another should be in readiness to take its place, and the treatment continued as long as may be necessary.

Bread-and-milk poultice is prepared by heating together sweet milk and bread deprived of its crust, and incorporating a little lard.

Mustard poultices differ from most of this class in preparation and in action. Pure mustard is used only in exceptional cases, when a prompt and strong action is desired. This is quite likely to blister the skin.

For ordinary cases the mustard is diluted with about an equal weight of flour, corn meal, flaxseed meal or other emollient, or with about half its volume of sodium bicarbonate. In the latter case a vigorous rubefacient action is produced, but the poultice seldom blisters. The mustard should be wet with lukewarm water, never with boiling water, since the action of the mustard is due to a volatile oil generated by the moisture, and this will not be formed if too much heat is applied.

In applying these, a thin cloth is usually placed between the moist mass and the skin, and staining thereby prevented.

The poultice is allowed to remain upon the skin from ten minutes to an hour or more, according to the demands of the case. The action is usually at its height in fifteen to twenty minutes, but a redness is produced in a shorter time. Upon very tender skins, or in cases of a weak system, a short action may be better than a protracted one.

Mustard poultices or plasters are also called **sinapisms**.

PLASMAS AND PASTES

Non-fatty bases, consisting of glycerin and water, thickened into a jelly-like mass with starch, gelatin or other agents, or pastes composed of starch or inert insoluble matters, with glycerin, water, soap or fats, have been recommended as substitutes for the fatty ointment bases.

They are about the consistence of ointments and have the advantage of greater cleanliness, easy removal from the skin and miscibility

with aqueous fluids. They are excellent solvents in themselves for many bodies. They do not become rancid, but they mould quickly, and unless some preservative agent is present, putrefaction soon begins. They become hard on exposure to the air, by evaporation.

A large proportion of glycerin prevents such changes; when this is absent some of the common antiseptic agents must be used.

Plasmas or jellies made from starch or gum do not melt like ointments when applied to the skin, and consequently medicinal matter is not as easily absorbed from them. Their chief use is as toilet preparations, or for superficial skin diseases, in which they serve an excellent purpose as cleansing, softening and cooling agents.

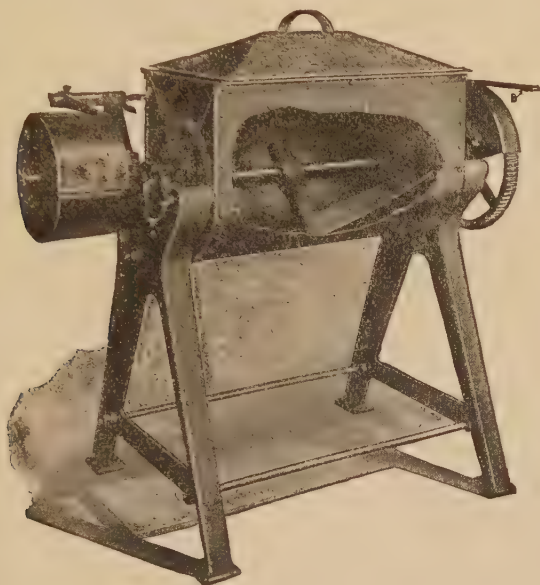


FIG. 67.—Paste mixer.

They are frequently perfumed, and when not designed for specific diseases are often sold under the name of "glycerin jellies," "emollient creams," etc.

Considered as toilet preparations, there are two classes of these in use; the true plasmas, opaque bodies, of which glycerite of starch and glycerite of tragacanth are types, and the transparent jellies, made from gelatin, chondrus, cetraria, agar-agar, etc.

The latter soften with heat or partially melt upon the skin, and are absorbed more readily. They should be made as thin and soft as possible without being fluid, and dispensed in collapsible tubes.

Glycerin jellies should contain at least one-half of their weight of water, since strong glycerin irritates the skin by abstracting water from it.

The gelatinizing agents in common use are:

Starch forms a jelly which is opaque when thick or translucent when thin.

Potato starch is most easily formed into a jelly, and is more translucent than most varieties.

The starch is first triturated with a little cold water to form a uniform mixture, then this is poured into boiling water, and the mixture boiled until the starch granules are fully swollen, usually about five minutes. If the starch be added directly to the boiling water it coheres into lumps which are not easily broken up, even on prolonged boiling.

The official glycerite of starch, which contains 10 per cent of corn starch, is a rather firm jelly. Particular care is needed in making this lest the mixture become overheated and the glycerin decomposed, thereby rendering it irritating.

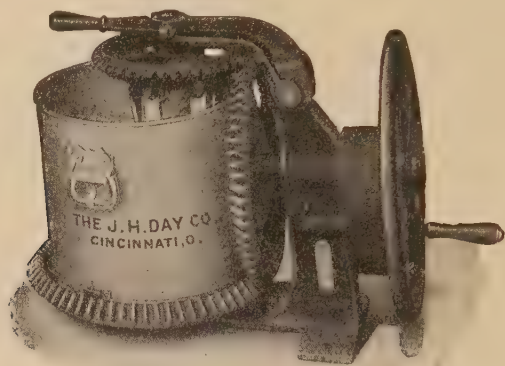


FIG. 68.—Hand paste mixer.

Tragacanth and Salep.—These are types of the gum-starches. They do not make transparent jellies, but resemble those made with starch.

Tragacanth makes a jelly in the proportion of five or six parts to one hundred, while only two to three parts of salep to one hundred are required. The process of the official mucilage of tragacanth is the best method of preparing a jelly with this.

Salep is first soaked in cold water, then this mixture is added to boiling water, and the boiling continued for a short time.

The National Dispensatory gives the following method of making salep jelly:

"Rub sixty grains of powdered salep with water in a mortar until it has swollen to four times its original bulk, then add gradually, and with stirring, a pint of boiling water, and boil down to eight ounces."

Chondrus and Cetraria.—These make very thick mucilages which are gelatinous when cold. Ten parts of the former or fifteen of the latter are required to make one hundred parts of stiff jelly. The moss is placed in a double amount of cold water and boiled half an hour, or until reduced to the required bulk. Much care is needed to prevent burning when the magma is thick, the least trace of which will make the jelly dark-colored.

When clear succulent pieces of moss are selected, a grayish-white translucent jelly is obtained. After boiling the mass is strained through cheese-cloth with pressure.

The mass is so thick that filtering is impossible, and a clear jelly cannot be obtained except by filtering a thin solution and then evaporating.

Cold water makes a thicker jelly with Irish moss than hot, but it is more granular and opaque and does not keep as well. The usual mucilage is made with boiling water because it is smoother and more permanent.

Agar-agar is the most powerful gelatinizing agent. It is prepared from several species of algæ growing in tropical waters.

One part of this makes a jelly with two hundred parts of water. It should be boiled about six hours, and filtered while hot. It filters readily when liquefied, but solidifies at 40° C., and in handling large quantities a hot filtration apparatus is needed.

It forms a very clear, firm jelly, and keeps fairly well if 10 per cent of glycerin be added. It is not as satisfactory as gelatin or chondrus, because it has a tendency to become watery or even to liquefy on standing, when it is made soft.

Gelatin comes next in power, requiring two to four parts for one hundred parts of jelly.

French "silver" or "gold-label" gelatin is best for pharmaceutical use. It dissolves easily in warm water, and usually gives a clear jelly by straining through cheese-cloth. It can be made to dissolve in glycerin by first softening with water, then heating with glycerin until dissolved and the water has passed off. The jellies containing water are apt to liquefy if stirred very much.

The solution of gelatin should be allowed to stand in a cool place to solidify, and, if not disturbed by stirring, it will keep growing firmer for a number of hours.

Isinglass resembles gelatin very closely; four parts of it make one hundred parts of clear tremulous jelly. It consists chiefly of a very pure gelatin, and is dissolved in the same manner. It is not easy, however, to obtain it of good quality.

By using larger proportions of any of these agents, stiff and rubber-like jellies may be prepared, suitable for making bougies, pencils, etc. Most of the jellies are hygroscopic, and should be preserved and dispensed in tight containers.

If made with agar-agar or gelatin, they should be clear and free from lumps.

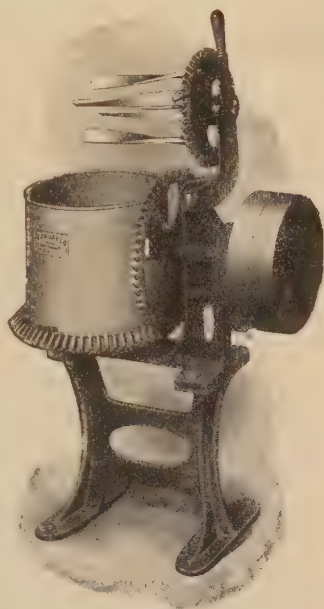


FIG. 69.—Day's power paste mixer.

They are easily moulded, when desired, and do not stick to the moulds. In all cases they should be allowed to set half an hour or longer in a cool place before dispensing.

In some cases they are used as paints, being melted and applied with a brush while hot. Thus used, they form a film upon the skin, which holds and protects the medicinal action, operating in the same manner as collodions.

Pastes are frequently used by dermatologists in preference to ointments for superficial skin diseases. They are usually pretty stiff in



FIG. 70.—Clips for collapsible tubes.

consistency and contain a large proportion of inert powders, as starch, kaolin, talcum, or chalk to produce the stiffness. The moistening agent may be glycerin, soft soap or petrolatum. In the kaolin paste (*Cataplasma Kaolini*), which is employed hot and as a substitute for a poultice, the glycerin, by its absorption of water, acts as a drawing agent.

The medicinal agents employed in this form are mostly astringents, antiseptics and emollients. (See *Pastæ Dermatologicæ*, N. F.)



FIG. 71.—Clip fastener for collapsible tubes.

Escharotic pastes were formerly used for caustic purposes, but have been superseded by the surgeon's knife, a desirable substitute in all cases when the patient will admit of it.

The preparation of pastes offers no special difficulties. The active agent is mixed with the diluent in the proportion desired, and the resulting mixture made into a soft paste by the addition of the moistening agent.

With very deliquescent substances like chloride of zinc, water must be used sparingly to avoid dissolving all of the salt and developing its causticity too strongly. The action of pastes is intended to be slow and gradual, and the salt should be in a condition of partial solution, except when the strongest action is desired. Escharotic pastes

may be very painful, and are sometimes mixed or moistened with anodynes to mitigate the pain. Alcohol and glycerin are also used as moistening agents for very soluble substances, while starch, calcium phosphate, plaster-of-paris and other inert substances may be used as diluents. These pastes are applied directly to the skin, or to the skin denuded of its cuticle by a blister, or by application of another caustic.

Caustics which are deliquescent have a tendency to spread, and this action on the surrounding tissues may be prevented by a dressing of simple cerate. This prevents the spreading of the caustic over the surface of the skin by capillary attraction.

CRAYONS OR PENCILS

Crayons or pencils are small pencil-shaped rods, usually measuring one to four inches in length, and one-fourth to three-eighths of an inch in diameter. They are intended for application to very small areas of surface, and are applied, after wetting the point or end, in the same manner as crayons. They need no dressings, and are largely used for the removal of small excrescences, or the treatment of very small areas.

They may consist entirely of the active agent, or of the agent in a diluted form.

They are prepared by fusion, or by combination with a suitable base.

Easily fusible salts, as silver nitrate and zinc chloride, or salts which melt easily in their water of crystallization, as zinc and copper sulphates, alum, etc., are simply melted and poured into suitable moulds. The moulds used for preparing urethral suppositories may be used for this purpose.

The pencils of lunar caustic and diluted nitrate of silver are familiar examples of these. The moulds should be warm to prevent too sudden congealing, and the liquid should be near its congealing point to obtain a smooth surface. The moulds should not be greased, but should be perfectly clean.

Salts that are melted in their water of crystallization must not be heated too long, lest a portion of the water be driven off. It is best to weigh these before melting, and again just before moulding, making up any loss in the second weighing by the addition of boiling water. A porcelain or metallic capsule or crucible is the best form of vessel in which to fuse the salts.

Silver nitrate pencils contain a small proportion (about 5 per cent) of chloride of silver (U. S. P.) or of potassium nitrate (Ph. Br.) to toughen them. If made from the pure salt, they are brittle and crystalline. A slight excess of nitric acid is sometimes also added to the melted salt to prevent discoloration.

If the melted salt is too hot when poured into the moulds, they are likely to be brittle and uneven as well as discolored.

Zinc chloride is seldom made into pencils, owing to its extreme deliquescence.

Copper sulphate may be moulded pure, or mixed with half its weight of powdered alum, and the mixture fused and moulded. Pencils of pure copper sulphate may also be formed out of selected crystals of the salt by turning in a lathe, or by filing.

For non-fusible bodies, when the active agent is desired only in a diluted condition, and when other medicaments than caustics are desired in the pencil form, a base or form must be used.

Gelatin makes a flexible pencil which is not easily broken, and which preserves the active agent in good condition. The jelly used for making these should be pretty stiff, containing 15 to 30 per cent of gelatin with some glycerin. The medicinal matter may be incorporated with the fluid before moulding, when the pencil will contain a definite proportion of it, or a pencil-form may be made of jelly,



FIG. 72.—Collapsible-tube filler.

which is coated with the active agent by rolling therein. In the latter case the pencil is moistened on the surface before rolling, unless the mass contains a considerable proportion of glycerin.

Gums, with starch or flour, make a stiff and hard pencil. They are moistened with a mixture of glycerin and water, the glycerin being necessary to prevent them from becoming so hard as to scratch the skin, and also to preserve them in a condition to yield up their medicinal matter readily. The gums employed are usually tragacanth and dextrin, the tragacanth furnishing a good body, and the dextrin

supplying the additional adhesive qualities needed. (See *Stili Medicamentorum N. F.*)

A **good general mixture** is tragacanth, 5 parts; dextrin, 30 parts; powdered sugar, 20 parts; and starch, 10 to 35 parts. The starch is used as a filler, and varied in quantity according to the proportion of active agent desired. Thus, for a pencil to contain 10 per cent of medicinal agent, 10 parts are added to the above quantities, while for 40 per cent of medicinal agent only 5 parts of starch, or better, 10 parts of starch and 15 parts of sugar can be used. The powdered ingredients are mixed intimately, and made into a stiff mass by the

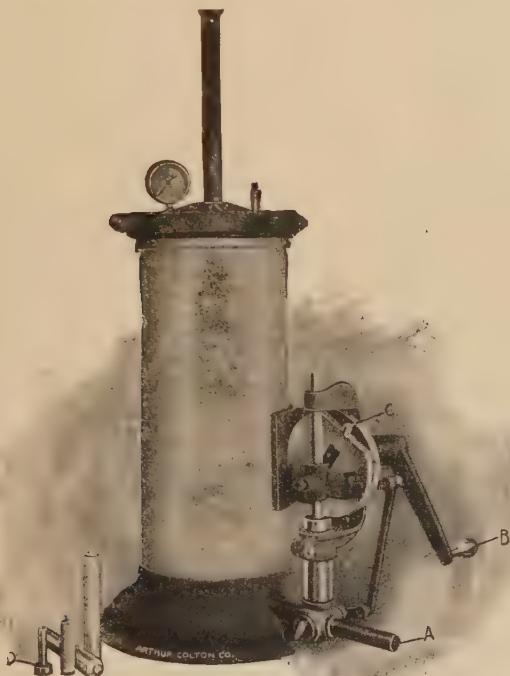


FIG. 73.—Collapsible-tube filler.

addition of a sufficient quantity of glycerin-water. The mass is then rolled into the desired form and dried. Unless otherwise specified the pencil may be made two and one-half inches in length and one-quarter inch in diameter. They should taper to a point at one end. They should be wrapped in tin-foil or paraffin paper, the label being affixed to one end. As with the gelatin pencils, the points or the surface to which they are applied, must be wetted before being applied.

Salve pencils are made of wax and hard fats, and should be firm enough to resist breaking, and yet soft enough to yield a film of their substance to the skin when rubbed upon it. They are larger than the soluble pencils, being one-half to three-quarters of an inch in diameter, and about two inches in length. They are made in the same

manner as suppositories, by either hot or cold process, and should contain only sweet and non-irritating fats. The same rules as those given for suppositories apply to these, except as regards melting-points, which may or may not be a consideration in pencils.

Pencils used for toilet and theatrical purposes are generally desired of high fusing-points.

MEDICATED DRESSINGS

Medicated Gauzes and Cottons are usually prepared by plaster manufacturers or special dealers, though their preparation is quite within the range of retail pharmacists.

They are generally understood to contain a certain percentage or quantity of medicinal agent in the finished gauze or cotton.

Besides this they may contain a small quantity of glycerin, or of oil and resin, to preserve a degree of softness and promote the activity of the medicinal agent.

To prepare them the compounds are dissolved in ether, alcohol or other volatile solvent; the glycerin, or rosin and a fixed oil, is added to this, then the mixture is thoroughly diffused through the gauze or cotton, then wrung out and dried. They must be dried quickly, but without heat. If allowed to remain in folds, or if not dried promptly, they are apt to become streaked. This can be prevented by wringing well, or by spreading out thinly, in a horizontal position, in a current of dry air.

If volatile ingredients are present, the gauze should be collected

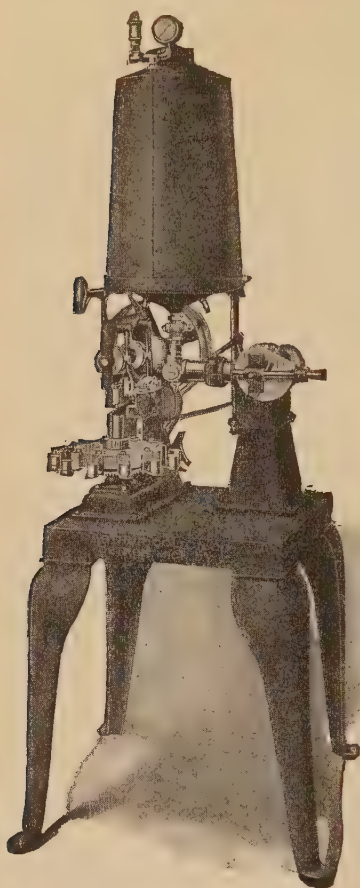


FIG. 74.—Collapsible tube filling and closing machine.

and preserved in tight containers as soon as the ether or alcohol has evaporated, or even before the last traces have disappeared. Since medicinal matter diffused in this manner is in a condition to change readily by action of air and light, or to evaporate if volatile, these preparations must be preserved in tight receptacles.

Furthermore, for their use in surgical dressings, pains should be taken to secure absolute cleanliness and to exclude disease or harmful germs.

In calculating the quantities of solution and of gauze required to obtain a gauze of definite percentage strength, allowance must be made for the additional weight of glycerin or of rosin and oil in the

solution, which is retained in the finished gauze. Thus the weight of the finished gauze will be the weight of the original gauze plus the total weight of the solids or non-volatile matter in the solution absorbed, and the weight of the medicinal agent must be in proportion to the total or final weight of the gauze, not simply to the gauze taken. (See note under iodoform gauze, No. 59.)

CATAPLASMS, PLASMAS, PASTES, PENCILS, MEDICATED DRESSINGS

1

Cataplasma Carbonis (Ph. Br.). Charcoal Poultice

- R. Powdered wood charcoal..... 1 ounce
Crumb of bread... 2 ounces
Linseed meal..... 1½ ounces
Boiling water..... 10 fluidounces

"Macerate the bread in the water for ten minutes near the fire, then mix; add the linseed meal gradually, stirring the ingredients that a soft poultice may be formed. Mix with this half the charcoal, and sprinkle the remainder upon the surface of the poultice."

2

Cataplasma Fermenti (Ph. Br.). Yeast Poultice

- R. Beer yeast..... 6 fluidounces
Wheaten flour.... 14 ounces
Water heated to 100° F..... 6 fluidounces

"Mix the yeast with the water, stir in the flour, and place near the fire till it rises."

3

Cataplasma Sinapis (Ph. Br.). Mustard Poultice

- R. Powdered mustard.... 2½ ounces
Lukewarm water 2 to 3 fluidounces
Mix.
Linseed meal..... 2½ ounces
Boiling water. 6 to 8 fluidounces
Mix.

Stir the two poultices together.

4

Cataplasma Sodæ Chlorinatæ (Ph. Br.). Chlorine Poultice

- R. Solution chlorinated soda..... 2 fluidounces
Linseed meal..... 4 ounces
Boiling water..... 8 fluidounces

Mix the linseed meal and boiling water, and add the soda solution.

5

Onion Poultice

- R. Onions, chopped fine.... 6 to 10
Rye meal... An equal quantity
Vinegar. Enough to make a paste

Mix the three and heat in a suitable pan, allowing the mixture to simmer about ten minutes, stirring frequently; apply hot, and renew frequently.

6

Spice Rubefacient

- R. Clove, ground..... ʒ iii
Saigon cinnamon, grd..... ʒ iii
Ginger, grd..... ʒ ii
Capsicum, grd..... ʒ ii
Hot vinegar..... q. s.

Mix the spices and moisten with enough hot vinegar to make a poultice.

7

- R. Tragacanth..... 6 Gm.
 Glycerin..... 18 Gm.
 Water, a sufficient quantity to make..... 100 Gm.

M. Sig.—Mucilage of tragacanth.

"Mix the glycerin with 75 cc. of water in a tared vessel, heat the mixture to boiling, add the tragacanth, and let it macerate during twenty-four hours, stirring occasionally. Then add enough water to make the mixture weigh 100 Gm., beat it so as to make it of uniform consistence, and strain it forcibly through muslin."

Make 20 Gm.

8

- R. Ichthyol 20.00
 Amyli..... 20.00
 Albuminis ovi, liquidi..... 0.75
 Aquæ destillatæ..... 60.00

M. Sig.—Ichthyol drying-liniment.

Boil the starch in the water until smooth, cool and incorporate the other ingredients.

9

- R. Pulv. tragacanthæ..... 1
 Sodii boratis..... 1
 Glycerini..... 36
 Aquæ rosæ..... 5

M. s. a. Sig.—Glycerin ointment.

Mix the gum thoroughly with the glycerin, heat and add the borax dissolved in the rose water.

10

- R. Starch..... 10 Gm.
 Water..... 20 cc.
 Glycerin..... 70 Gm.

M. Sig.—Glycerite of starch.

"To the starch, contained in a porcelain dish, add the water and mix well, then pour this into the glycerin heated to 140° C. (284° F.), and not exceeding 144° C. (291° F.), stirring constantly and continue the heat until a translucent jelly is formed. Transfer the product to suitable vessels, provided with well-fitting covers."

Make one-fifth the quantity.

11

- R. Amyli..... 3 ij
 Aquæ..... 3 x

M. Sig.—Mucilage of starch, B. P.

Triturate the starch with the water, gradually added, then boil for a few minutes, constantly stirring.

12

- R. Calomelatis 1.0
 Acidi tannici..... 1.0
 Glyceriti amyli..... 30.0

M. Sig.—Calomel and tannin plasma.

13

- R. Zinci oxidi..... 10.0
 Acidi salicylici..... 0.2
 Glyceriti amyli..... 10.0

M. Sig.—Apply as needed.

14

- R. Sulphuris..... 10.0
 Tinct. benzoini..... 10.0
 Mucilaginis amyli..... 80.0

M. Sig.—For external use.

15

- R. Zinci oxidi..... 25.0 Gm.
 Calcii carb. præcip..... 25.0 Gm.
 Acidi oleici..... 2.5 Gm.
 Olei lini..... 25.0 Gm.
 Liq. calcii hydrox..... 22.5 Gm.

M. Sig.—Unna's soft zinc paste.

Triturate the zinc oxide and calcium carbonate to a smooth mixture with the oleic acid and linseed oil, and gradually incorporate the lime water.

16

R.	Acid salicylici.....	2
	Zinci oxidi,	
	Ampli.....aa	24
	Petrolati albi.....	50
M.	Sig.—Lassar's zinc paste.	

18

R.	Kaolini.....	56.5 Gm.
	Acidi borici.....	4.5 Gm.
	Methylis salicylatis....	0.2 cc.
	Thymolis.....	0.5 Gm.
	Oil of peppermint.....	0.5 cc.
	Glycerini.....	38.7 Gm.
	Sig.—Kaolin cataplasm.	

19

R.	Gelatini.....	2.0
	Glycerini.....	50.0
	Aquæ.....	35.0
M.	Sig.—Glycerin jelly.	

Add the gelatin to the water and heat on a water-bath until completely liquefied, then add the glycerin, mix well and pour into bottles to cool and solidify; or put, when cold, into collapsible tubes.

20

R.	Gelatini glycerinati.....	20
	Glycerini.....	35
	Acidi salicylici.....	10
	Aquæ destillatæ.....	35
Misce.	Ft. gelatina.	
	Sig.—Salicylic glycerogelatin.	

Melt the glycerinated gelatin and add the glycerin and water in which the salicylic acid has been dissolved.

21

R.	Gelatini glycerinati.....	30
	Glycerini.....	25
	Aquæ destillatæ.....	35
	Zinci oxidi.....	10
Misce.	Ft. gelatina.	
	Sig.—Hard zinc glycerogelatin.	

Melt the glycerogelatin and stir in the glycerin with which the zinc oxide has been triturated, then add the water and stir until the mixture sets.

22

R.	Gelatini glycerinati.....	20
	Glycerini.....	35
	Aquæ destillatæ.....	25
	Zinci oxidi.....	10
Misce.	Ft. gelatina.	
	Sig.—Soft zinc glycerogelatin.	

23

R.	Gelatini.....	10
	Albuminis ovi.....	20
	Acidi salicylici.....	1
	Aquæ rosæ.....	225
	Glycerini.....	250
M.	Sig.—"Glycerin jelly."	

Dissolve the gelatin in the rose-water by aid of a very gentle heat. Let cool and before it jellifies stir in the albumen. Dissolve the salicylic acid in the glycerin, and after again warming the gelatin solution add it to the latter, stirring constantly. When well mixed strain into gallipots or wide-mouthed bottles and allow it to gelatinize.
(Used for chapped lips and hands, blisters, etc.)

- 24
- R. Gelatini..... 4 Melt the gelatin in the water by aid of
 Zinci oxidi..... 3 heat, add the glycerin and *sift* in the
 Glycerini..... 5 zinc oxide; strain through cheese-cloth
 Aquæ..... 9 and stir until it begins to thicken.
 M. s. a. Sig.—“Unna's glycerin
 jelly.” (When required for use a portion is
 melted and applied with a brush.)

- 25
- R. Glycerini..... 24 Heat the starch, glycerin and water
 Amyli..... 3 until a transparent jelly is obtained,
 Tinct. arnicæ..... 4 and when cold incorporate the arnica.
 Aquæ..... 6
 M. Sig.—Arnica jelly.

- 26
- R. Adipis lanæ hydros..... 10 Dissolve the gelatin in 75 parts of hot
 Tinct. quillajæ..... 20 water and strain.
 Olei amygdal. exp..... 10 Emulsify the lanolin and oil with the
 Gelatini..... 4 tincture of quillajæ in a warm mortar,
 Aquæ fervent..... q. s. add the warm gelatin solution and stir
 M. Ft. gelatinum. until the mixture thickens.
 Sig.—“Lanolin paste.” Set aside to cool.

- 27
- R. Gelatin chondri,
 Glycerin..... aa 25 Prepare the chondrus jelly by boiling
 M. 5 Gm. of the moss with 200 cc. of
 water down to 25 cc.; when strained,
 add the glycerin while warm, and place
 in wide-mouthed bottles, or jars, to
 stiffen.

- 28
- R. Cydonii contusi..... 4.0 Macerate the quince seed in the water
 Aquæ bullientis..... 400.0 for 12 hours, strain and add the glycerin
 Sodii boratis..... 4.0 and borax. Gradually add the spirit,
 Glycerini..... 60.0 in which the oil has been dissolved, and
 Spiritus camphoræ..... 30.0 mix thoroughly.
 Ol. amygdalæ amaræ..... 0.60
 M. Sig.—“Camphor cream.”

- 29
- R. Saponis..... 12 Shave the soap very fine, place in
 Benzini..... 38 6-inch capsule, cover with 45 cc.
 Aquæ ammon. fort..... 38 water, and heat on a water-bath until
 Aquæ..... q. s. the soap is soft and jelly-like. Add
 M. Sig.—“Benzine jelly.” water to make 45 Gm. of mixture,
 mix well and squeeze through cheese-
 cloth into 4-ounce, wide-mouthed bottle.
 Add the benzine, shake together,
 then gradually add the stronger water
 of ammonia, constantly shaking.

30

- R. Benzini..... 5 j
 Tinct. quillajæ..... 5 ss
 M. Sig.—“Benzine jelly.”

31

- R. Benzini..... 5 j
 Tinct. quillajæ..... 5 ij
 Aquæ ammoniæ fortioris..... 5 ij
 M. Sig.—Benzine jelly.

32

- R. Iodoformi..... 10
 Gelatini..... 10
 Glycerogelatini..... 15
 Aquæ destillatæ..... 65
 M. Sig.—Unna's iodoform gelatin.

33

- R. Iodi..... gr. 1/12
 Gelatini glycerinat..... 5 i
 M. s. a. Mitte tales xxx no.
 Sig.—Iodine cubes.

34

- R. Glycerogelatini zinci oxidi,
 10 per cent..... 100
- Dissolve 15 Gm. of gelatin in 35 parts of water and 25 parts of glycerin, by heat. Levigate 10 Gm. of zinc oxide with 15 Gm. of glycerin, add to the gelatin solution and pour into chilled moulds.

35

- R. Acidi salicylici..... 10
 Creosoti..... 20
 Ceræ flavæ..... 5
 Sevi benzoinati..... 65
 Misce. Ft. Steatina.
 Sig.—Caustic salve-mull.

36

- R. Zinci oxidi..... 10
 Sevi benzoinati..... 70
 Adipis benzoinati..... 20
 Misce. Ft. steatina.
 Sig.—Zinc salve-mull.

37

- R. Hydrargyri bichlorid..... 0.2
 Alcoholis..... 6.0
 Sevi benzoinati..... 90.0
 Adipis benzoinati..... 5.0
 Misce. Ft. steatina.
 Sig.—Mercuric chloride salve-mull.

Dissolve the bichloride in the alcohol and incorporate in the fats.

38

- R. Balsami peruviani,
 Iodoformi..... āā 5 ij
 Glycerini..... 3 xiv
 M. Ft. unguent.

A solid paste results on mixing. A peculiar mixture.

39

- R. Zinci chloridi..... 20
 Amyli..... 20
 Zinci oxidi..... 5
 M. Ft. escharotica.
 Sig.—Chloride of zinc paste.

Mass with water, and roll rapidly into cones, which are then rolled in talc.

40

- R. Zinci oxidi..... 20.0
 Cretæ præparatæ..... 10.0
 Liq. plumbi subacet..... 10.0
 Olei lini..... 10.0
 M. Sig.—Zinc-lead paste.

Shake together the lead water and oil, and stir into this mixture the powders, taking care to thoroughly mix.

41

- R. Acidi sulphurici,
 Carbonis ligni..... āā p. e. q. s.
 M. Ft. pasta.
 Sig.—Acid cautery paste.

42

- R. Acidi arsenosi..... gr. ij
 Morphinæ sulphatis..... gr. j
 Creosoti..... q. s.
 M. Ft. pasta.

43

R.	Farinæ tritici.....	30.0
	Phosphori	2.5
	Aquæ.....	15.0
	Syr. fusci.....	30.0
	Barii carbonat.....	15.0
	Adipis.....	15.0

M. s. a. Sig.—*Rat paste.*

Make a dough with the flour and water, and incorporate the lard.

Place the molasses in a wide-mouth bottle, add the phosphorus and heat upon a water-bath until the latter is melted, stir well to suspend the phosphorus, and then add to the dough and incorporate quickly. Finally stir in the barium carbonate and bottle.

(CAUTION.—The mass is liable to take fire while incorporating the phosphorus, which should be done in an open space, the hands being protected by wrapping in wet cloths.)

44

R.	Acidi salicylici.....	4.0
	Ceræ albæ.....	5.0
	Adipis lanæ hydros.....	11.0

M. Ft. stili.

Sig.—Salicylic acid pencils.

46

R.	Iodoformi.....	2
	Zinc oxidi.....	1
	Olei theobromatis.....	6
	Ceræ flavæ.....	5
	Tragacanthæ.....	4

M. Ft. bouginariæ, vi. no.

Sig.—Iodoform crayons.

48

R.	Ichthyol.....	4
	Tragacanth. pulv.....	1
	Amyli.....	6
	Dextrini.....	7
	Sacchari pulv.....	2

M. Ft. stili. Sig.—“Ichthyol pencils.”

50

R.	Iodoformi.....	8
	Resinæ.....	1
	Ceræ flavæ.....	6
	Olei olivæ.....	5

M. Ft. stili.

Sig.—Forty per cent iodoform pencils.

45

R.	Acid salicylic.....	10
	Tragacanthæ.....	5
	Amyli.....	30
	Dextrini alb.....	35
	Sacchari.....	20
	Aquæ.....	q. s.

Misce. Ft. stili xv no.

Sig.—Salicylic acid pencils.

47

R.	Iodoformi.....	3 jj
	Amyli.....	3 ii
	Tragacanthæ.....	3 j
	Dextrini.....	3 j
	Sacchari.....	3 ss
	Glycerini.....	
	Aquæ.....	aa q. s.

M. Fac. stilos xij no.

Sig.—Iodoform pencils.

49

R.	Acidi carbolici.....	2
	Resinæ.....	4
	Ceræ flavæ.....	8
	Olei olivæ.....	6

M. Ft. stili.

Sig.—“Carbolic acid pencils.”

51

R.	Carbonis ligni.....	30.0
	Potassii nitratis.....	4.0
	Ferri alcoholisati.....	5.0
	Benzoini.....	1.0
	Mucilag. acaciæ.....	q. s.

M. Ft. styli.

Sig.—Moxas, or cauterizing pencils. To be ignited and applied.

(Ferrum alcoholisatum—“alcoholized,” —i. e., powdered iron.)

52

R.	Petrolati liquidi.....	58.4	cc.
	Acidi oleici.....	30.0	cc.
	Ol. lavandulæ.....	0.5	cc.
	Aquæ ammon. fort.....	5.0	cc.
	Alcoholis.....ad.	100.00	cc.

Misce s. a. Sig.—Liquid petroxolin.

Mix in the order written, and warm until the liquid becomes clear.

53

R.	Sulphuris.....	3	Gm.
	Olei lini.....	37	Gm.
	Acidi oleici.....	30	Gm.
	Petroxolini liquidi.....ad.	100	Gm

M. Sig.—Sulphur petroxolin.

Dissolve the sulphur in the linseed oil by aid of heat, and add the oleic acid and petroxolin.

54

R.	Acidi salicylici.....	5	i
	Pilocarpinæ muriat.....	gr. x	
	Hydrargyri bichloridi.....	gr. i	
	Olei ricini.....	3	i
	Alcoholis.....	3	i
	Aquæ.....q. s. ad.	3	iv

M. Sig.—Apply to the scalp as directed.

Emulsify the castor oil with two drachms of tincture of quillaja.

55

R.	Iodoformi.....	gr. xv	
	Ether.....	3	iss
	25 per cent alcohol.....ad.	3	iss

Water cannot be used. Dissolve the iodoform in the ether, add 3 drachms of alcohol, then enough castor oil to make 1 1/2 oz.

56

R.	Resorcinolis.....	gr. xx	
	Zinci oxidi.....	3	iv
	Acidi borici.....	gr. xx	
	Lanolini.....	3	iv
	Olei olivæ.....	3	ii
	Liq. calcii hydrox.....ad.	3	viii

M.

Dissolve the resorcinol in 5 1/2 oz. of lime water, add the olive oil and shake well. Mix the zinc oxide with the lanolin and gradually incorporate with the oil mixture. Finally add the boric acid.

57

R.	Camphoræ.....	gr. ii	
	Mentholis.....	gr. iv	
	Cocainæ hydrochlor.....	gr. v	
	Petrolati liquidi.....	3	iv

M.

Use 4 1/2 grains of cocaine alkaloid.

58

Carbasus Carbolata (Carbolized Gauze)

R.	Resin, in coarse powder	40	parts
	Castor oil.....	5	parts
	Carbolic acid.....	10	parts
	Alcohol.....	225	parts
	Gauze muslin, a sufficient quantity.		

Dissolve the resin, castor oil and carbolic acid in the alcohol. Then immerse in the mixture loosely folded pieces of gauze-muslin, allow them to become thoroughly saturated, then take them out and press out the excess of liquid until the weight of the impregnated gauze amounts to 170 parts for each 100 parts of original fabric. Spread out the pieces horizontally, and as soon as the alcohol has nearly all evaporated, fold and wrap the pieces in paraffin paper and preserve them in air-tight receptacles. The impregnated gauze, when dry, contains about 2.5 per cent of carbolic acid.

59

Carbasus Iodoformata (Iodoform Gauze)

R. Iodoform.....	10 parts
Ether.....	40 parts
Alcohol.....	40 parts
Tincture of benzoin.....	5 parts
Glycerin.....	5 parts
Gauze muslin, a sufficient quantity.	

Dissolve the iodoform in the ether and add the alcohol, tincture of benzoin and glycerin. Immerse in a weighed quantity of this solution, contained in a suitable vessel, the exact amount of gauze required to absorb the whole of it, to produce a product of a prescribed percentage of iodoform, work it about with a pestle so as to impregnate it uniformly; then take it out, hang it up in a horizontal position to dry, and in a dark place. Lastly wrap it in paraffin paper and preserve it in air-tight receptacles.

NOTE.—To calculate the amount of muslin and of iodoform solution required to obtain a product approximately of any required percentage of iodoform, let x denote this required percentage. Then take of the above iodoform solution ten times this quantity (or $10x$). Also multiply the required percentage (x) by three, divide the neutral product by two and subtract the quotient from 100 $\left(100 - \frac{3x}{2}\right)$. The remainder represents the number of parts by weight of gauze-muslin to be used.

60

Gossypium Stypticum, N. F. (Styptic Cotton)

Purified cotton.....	100 Gm.
Solution of chloride of iron. 80 cc.	
Glycerin.....	16 cc.
Water.....	225 cc.

Mix the liquids, immerse the cotton in the mixture and allow to remain one hour. Then remove it, press it until it has been brought to weight of 300 Gm., spread it out in thin layers, in a warm place, protected from dust and light, and when it is sufficiently dry transfer it to well-closed receptacles.

State Board Prescriptions

I	
R. Zinci oxidi.....	10.0
Calcii carbonat.....	10.0
Olei lini.....	10.0
Liquoris calcis.....	10.0
Misc. Fiat pasta zinci mollis. N. F.	
Mitte. $\frac{5}{i}$.	
Sig.—Use as directed. (Mass. and Ohio.)	

2	
R. Hydrarg. oxid. flav.....	10
Acid oleici.....	30
M. S. a. (Fla.)	

3

R. Mentholis.....	0.3
Puly. camphoræ.....	0.6
Olei eucalypti.....	0.3
Petrolati liq. ad.....	30.0
M. Sig.—Applicandum ter in die.	
(N. Y.)	

CHAPTER XV

STERILIZATION AND DISINFECTION

Modern methods of medical and surgical treatment demand that the pharmacist shall appreciate the value of antiseptic agents and preparations in the treatment of diseases. The science of bacteriology has changed the methods of treatment, in some instances radically, and frequently the composition of the preparation is secondary in importance to its condition and the way it was prepared. For since most diseases are now known to be caused by germs, in one form or another, the destruction of germs or their elimination have come to be regarded as matters of first importance. Hence the large use of antiseptic agents at the present time.

While the value of sterilization is universally recognized, the specific conditions which demand it will be found to vary in the judgment of physicians. Some are very particular about it at all times, while others are indifferent toward it except in special cases. From business motives, the pharmacist should be prepared to supply exactly what is wanted without thought as to whether the desire is consistent or not. A pleased physician is many times a pleased customer.

The germs which cause disease are known according to their form and characteristics, as

Bacteria, a general term applying to all those which are concerned in the disease-producing and putrefactive processes. According to their shape they are divided into

Bacilli, those having the form of a rod. Some of these have the power of motion in fluids, and are called **motile**.

Micrococci or Cocci, a globular form, appearing like small dots under a microscope. The diseases in which pus is formed are caused mostly by this class. According as the micrococci are grouped, they are known as **diplococci**, in groups of two, **tetrads**, in groups of four, **streptococci**, in chains of indefinite number, **staphylococci**, in clusters, **sarcinæ** in solid cubical masses.

Spirilla or Vibrios, rod-shaped organisms, having a curved form and appearing something like minute worms.

Only a small proportion of the known germs cause diseases, and those which do are called **pathogenic** bacteria, while those which are regarded as harmless to the human system are termed **non-pathogenic**.

A somewhat higher order of organisms are the **fungi** and **yeasts** which are the cause of putrefaction and fermentative processes. These are one of the lowest forms of vegetable life, and are reproduced either sexually, or non-sexually by budding or fissure. They contain no chlorophyll and are dependent for their food upon dead or living organic matter obtained from the higher orders of plants or animals. They are familiar as the common **moulds** or **mildews** (of which they are a variety of species) or as yeasts.

They are the primary causes of decay or of fermentation, and in a very few instances they are the cause of disease. Familiar instances of them are the cheese-mould (*Penicillium Glaucum*) which is present everywhere, and is carried about by currents of air until it finds lodgment and a chance to develop. It is a troublesome fungus to the bacteriologist, often spoiling his cultures by contamination or by crowding out other germs. Others are the fungus of sour milk and sour bread (*Oidium Lactis*) and of vegetable putrefaction (*Aspergillus Niger*) a variety of which can grow on animal organisms and produce disease and death. The skin diseases *favus* and *ring-worm*, and the ear-disease *otomycosis* are caused by fungi. There are a number that cause disease in fish, insects and animals.

But to the pharmacist they may be troublesome as the cause of decay in moist drugs, or as the cause of fermentative or putrefactive changes in syrups, alkaloidal solutions, infusions, aqueous extracts, etc. These moulds or yeasts are very difficult to exclude, since they are everywhere present. Many are too small to be filtered out by the ordinary methods of filtration, but are easily killed by heat. Others are large and can be filtered out. The number of known species of fungi is estimated at 30,000 and includes the edible mushrooms and truffles to the poisonous ergot, and the pathogenic tinea. Some are commercially valuable, as yeast, some produce useful products under favorable development, as diastase, lactic and citric acids, etc. But all are troublesome when out of place.

Besides the bacteria, some diseases are caused by **protozoa**, organisms which belong to the animal kingdom. They are of irregular form, pass through a complex cycle of development, and are related to the amoeba of our fresh-water ponds. Malaria, tropical dysentery, and probably other diseases are caused by them.

All these germs require favorable conditions of moisture, food, and temperature for the sustenance of life, and may be very sensitive to changes in their environment. They are extremely minute, many of them being less than one-twenty-five-thousandth of an inch in diameter, so the necessary moisture and food may be found in places where the eye would see nothing. When dried, some die and some lie dormant like seeds. In fact some have a definite seed form, known as **spores**, which resist drying and destruction to a marked degree. Fortunately the most of the pathogenic bacteria do not form spores, and so are the more easily killed.

While the non-pathogenic germs are in themselves harmless in solutions or if introduced into the system, yet in their development they may form products which are harmful, or they may decompose active medicinal bodies, such as alkaloids, using them up as food. Hence it is frequently necessary to sterilize a liquid which is to be kept for some time, while a similar solution used immediately would not need to be so treated.

A body is sterilized when all germs of any sort are killed, including spores. Sterilization means the destruction of all life, usually by heat. A body is **disinfected** when all germs contained in it have been killed or rendered innocuous by the use of germicides.

The term **disinfection** is most commonly applied to the process of destroying germs which may be present in houses, ships, clothing,

bales of rags, cotton, furniture, etc., which have been in contact with cases of contagious diseases, or in destroying the organisms on the hands in preparing for an operation.

Bodies which are entirely free from living germs are termed **aseptic**.

Now while complete asepsis is not necessary in all medical treatment, it is evident that all articles used in a sick-room should be free from pathogenic germs, at least.

Sterilization is required for special conditions, or for specific purposes. It is therefore the special article that the pharmacist may be called upon to sterilize, and it may be that the demand is so rare that the process seems unimportant. But it is just the special demand that counts the most when it is supplied.

Disinfection and sterilization are accomplished by physical agents, by chemical agents, or by mechanical means, particularly filtration. The physical agents are heat, sunlight, electricity and ultra-violet rays. Of these heat is the most commonly used. Sunlight is effective with longer exposures and is nature's means of purifying water and air, but requires several hours. Electricity demands a special apparatus and is not much used. Electrical ozonizers, which are apparatuses for the generation of ozone electrically, have been put upon the market with great claims for efficiency, but they have not proved successful, ozone not being as powerful as was imagined. The use of ultra-violet light has come into prominence, particularly for sterilizing water, and is both economical and efficient when properly used. The rays are generated by a mercury arc in a quartz tube, because glass cuts them off in part. The rays are not very penetrating and are cut off by suspended solids so that this means is only effective on perfectly clear and not deeply colored liquids. It has the advantage of not introducing any foreign matter or of inducing change by heat, and is increasing in importance as better apparatuses are adapted to its use.

In the use of chemical agents we are restricted to such as do not harm the substance which is sterilized, and further to those which do not interfere with the purposes of the article, or be objectionable if taken or applied themselves. Thus it would not do to use for sterilizing a medicinal preparation, a substance which is itself poisonous or irritating.

Next to the choice of an agent comes the question of the strength in which it should be employed.

Partial disinfection is often sufficient for certain treatments. When chemical agents are used in quantity just sufficient to inhibit the growth of germs without entirely destroying them, they are termed **antiseptics**, and the process **antiseptis**. In such cases it is intended that all pathogenic germs which are likely to be present shall be killed, but that non-pathogenic germs shall only be prevented from multiplying.

This may be accomplished either by the use of agents which are not powerful enough to kill all germs and their spores, but which may kill the more sensitive and reduce the vitality of the rest, or it may be accomplished by the use of powerful disinfectants used in solution too weak to destroy all the germs present. The same substance may therefore act as an antiseptic in weak solutions, and as a disinfectant in strong solutions.

A disinfectant must kill the germs and must act quickly.

An antiseptic may not kill the germs but it prevents their growth and development; it must therefore act continuously. A chemical which acts by decomposition may be a good disinfectant but it is not a good antiseptic because its action is temporary.

The medium in which it is employed also makes a difference. For instance, distilled water, if perfectly pure, will act as a germicide by starving the bacteria, but it is never pure enough to accomplish this completely. Pond or river water, containing organic matter, will furnish food and favorable conditions for their development, and a solution of peptone or albumen is still more favorable. Thus it would take a larger proportion of any agent to sterilize a beef extract or an organic solution, than to sterilize the same quantity of distilled water. Besides organic matters, weak solutions of salt and phosphates are favorable to germ life.

The propagation of germs under favorable conditions is extremely rapid. It is estimated that a single germ will produce fifteen to twenty-five *millions* of germs in twenty-four hours. Thus we can never count on there being only a few germs present to kill.

Combinations of disinfectants sometimes increase the power of each, and sometimes decrease it. They must be combined intelligently if at all. Different germs also differ in their vital resistance. In general, the pathogenic bacteria are more easily killed than the non-pathogenic. Heat adds to the power of the disinfectant.

Heat, whenever it does not injure the article, is a preferred means of sterilizing, particularly for pharmaceutical preparations, because it does not introduce any foreign substance. Unfortunately, heat injures many of the most active medicinal agents, and its use is thus restricted.

Dry heat is less effective than moist heat at the same temperature, but it can be employed at much higher temperatures, even up to that of flame, and so is preferred where it can be used. It is, of course, applied only to dry bodies. The temperature needed is 150° – 170° C., or just under that at which cotton turns brown. For most articles this temperature maintained for two hours is sufficient. An ordinary stove-oven, or an oil-stove oven is all the apparatus needed.

Dry heat is the most convenient way of sterilizing bottles, ointment-jars, flasks, funnels, or other containers or implements. If the bottles are stoppered with cotton while being sterilized, they will remain sterile so long as the cotton remains in place. A supply sufficient for a long time may thus be sterilized in one operation.

Spatulas, glass rods, and small articles, which will bear a sudden direct heat, may be quickly sterilized by passing through a non-luminous flame two or three times. They do not need to be held in the flame, but simply exposed for an instant to the direct heat of the flame. It is safer to pass them through the flame two or three times in succession.

Moist heat is applied to all liquid bodies, and sometimes to dry substances. It is most effectively and economically applied as moist steam, in a protected chamber, as in the Arnold or Koch sterilizers. These, in the small sizes particularly, are inexpensive apparatuses, and where the operation is frequently performed, well repay their cost.

The steam-cookers made for culinary purposes can be used just as effectively but less economically. But the operation can also be performed by subjecting the body to be sterilized to the full heat of boiling water. Thus an ounce of solution may be rendered innocuous by hanging the bottle containing it, stoppered with cotton, in a dish of boiling water. The time required for complete sterilization is about 30 minutes, except in the case of certain spore-bearing bacilli which may resist several hours' boiling. Unless these are supposed to be present, 30 minutes is sufficient. The time is to be reckoned, not from the moment when the article is placed in the steam or boiling water, but from the time when it has attained the full temperature. A small body will heat quickly and need be kept in the steam but a few minutes more than the required time, but a large quantity will need to remain enough longer to allow for its initial heating.

The surest method of sterilizing is to heat the object in steam for 30 minutes on three successive days. The object of successive, intermittent heating, is to allow for the killing of the spores, and this method of fractional sterilization is only applicable to those substances which contain such a food supply as will make the spores develop. In the first heating, the active, vegetating germs are killed, but not the spores. During the succeeding twenty-four hours the spores germinate but do not have time to form new spores, and in the second heating these are killed. The third heating is to insure the completion of the process. Solutions sterilized in this way will keep indefinitely without change. This method is termed **intermittent sterilization or tyndallizing**.

In sterilizing any fluid it is to be remembered that the bottle and the cork are also to be sterilized. Rubber stoppers are best to use, because they do not lose their elasticity during the process, as do corks. Everything is covered with germs, and it is easy to contaminate a liquid after sterilizing it. Subsequent transferring to another bottle, the insertion of a new stopper, filtering, etc., will introduce fresh organisms into a sterile solution, and undo the work already done. These things must be considered in advance, and the sterilization must be the last operation. As Dr. Rosenau says of disinfection, "germs are little things, and it is little things that count in this work." Work of this kind must be thoroughly done, or it were better not to attempt it. It is a simple operation, but it requires infinite care.

Pasteurizing is heating to about 60° C. (140° F.) and is applied to bodies which would be injured by the temperature of boiling water. It is, of course, not as efficient as boiling or steaming, but it is sufficient to kill most pathogenic germs. When repeated twice, at intervals of about twenty-four hours, it is very effective. All bodies which are injured by high heat, such as alkaloids or preparations of ergot, coca, belladonna, etc., should be pasteurized, if sterilization is required in them.

Chemical Agents.—Certain chemicals, particularly those that act upon or unite with albumen, are very active as germicides. Most chemicals will destroy germs in concentrated solutions, but a chemical can be properly called a germicide only when it kills the germs in comparatively weak solutions.

The strength of the solution is important in any case. Thus a solution of mercuric chloride of the strength of 1 to 15,000 will prevent the growth of all bacteria, but a strength of 1 to 1,000 is required to kill all germs and spores. Likewise a solution of formalin of the strength of 1 to 50,000 will prevent the development of most bacteria but a strength of 1 to 100 is required to kill.

Time is also required to kill germs, and the more numerous the germs, or the weaker the solution, the longer must be the contact. None are killed instantly, and the simple dipping of an article into a disinfecting solution is not sufficient. From a few minutes to several days may be required, according to the strength of the solution, the power of the germicide and the resistance of the bacteria. Temperature is another factor in the case. All chemical solutions act more powerfully when warm, and even a rise of but ten degrees in temperature may very materially increase the power of a solution. A moderate heat will multiply the power of any chemical germicide many times beyond that of room temperature. It is therefore recommended to use chemical solutions at least moderately warm, whenever possible.

The exact antiseptic power of any chemical agent is a matter of time, temperature, and the character of the germs present. The following table by McFarland shows the proportions in which vitality is inhibited under ordinary conditions of temperature, and for general purposes may be considered sufficient for pharmaceutical preparations wherever they may be suitable.

Hydrogen peroxide,	antiseptic in 1:20,000
Formalin,	" " 1:25,000 to 1:5,000
Mercuric chloride,	" " 1:14,300
Silver nitrate,	" " 1:12,500
Methyl violet,	" " 1:5,000 (1:2,000,000)
Creolin,	" " 1:5,000
Thymol,	" " 1:1,340
Salicylic acid,	" " 1:1,000
Benzoic acid,	" " 1:900
Zinc chloride,	" " 1:525
Potassium permanganate,	" " 1:285 (not prompt in action)
Boric acid,	" " 1:143
Chloral,	" " 1:107
Ferrous sulphate,	" " 1:90
Creosote,	" " 1:20
Carbolic acid,	" " 1:20 to 1:50
Alcohol,	" " 1:10
Eucalyptol,	" " 1:5

For the purpose of assisting in sterilization or of protecting substances from subsequent contamination, chemical agents are employed. Such agents should be used only with the consent of the physician who is to be responsible for their administration, and the other precautionary measures should not be neglected.

Dependence solely upon chemical germicides demands larger proportions of these than is usually allowable, hence they should be used as adjuncts only, and generally in quantities insufficient to insure sterility in themselves.

For comparing the relative value of disinfectants and antiseptics, phenol is commonly used as the unit, and the value is expressed in

numbers which are termed the **phenol coefficient**. This number is obtained by comparing the amount of germicide with phenol in the minimum quantities needed to kill certain bacteria. The test must be made on specified germs, under rigid conditions of temperature, technique, strength and adjustment of the medium, and even of the strain of bacteria. Slight changes in technique, in the alkalinity of the medium, the strength or even the strain of the bacteria, etc., will make a material difference in the phenol coefficient. The bacterium usually employed is that of typhosus, and the method used is that of Rideal and Walker, or the U. S. Hygienic Laboratory,—or such individual modifications as can carry weight and be accepted. But the agents have greatly different action on different germs. For instance the mild silver-protein compounds have a low phenol coefficient when tested by the standard methods on typhosus bacteria, but would have a high coefficient if tested on gonococcus. Since these agents are not used in typhus, but are used in gonococcic infections the phenol coefficient does not indicate the value at all. Thus when eugenol is said to have a phenol coefficient of 10, indicating that it is ten times as strong as phenol in germicidal action, it must be remembered that this applies only to the specific germ, and under the specific conditions and technique of the test by which it was compared. Its value as a germicide or antiseptic might be almost reversed when compared on some other germ or under other conditions. The statements of comparative antiseptic value of different agents are therefore not to be taken as universal or altogether dependable, but only as suggestive relations, based on the standard methods of comparison. Bacteriologists are trying to find a more satisfactory method of comparing antiseptics, but there are so many factors involved that it is very difficult to find any one method which would be generally satisfactory.

When chemical agents are employed, the usual precautions should be observed as to cleansing and sterilizing bottles, graduates, stoppers, etc., and in so far as possible without injury, the substance itself should be sterilized or pasteurized by heat. The chemical agents should only be used to assist in the processes and to hinder subsequent contamination.

It is impossible to set definite limits which will fit all cases for the amounts of the agents which may be employed, because the composition of the substance and its degree of contamination are important factors in sterilization.

Solutions of salts, practically free from organic matter, are easily sterilized, while solutions which contain appreciable, though small, amounts of organic substances may be difficult to sterilize.

Mineral acids, while objectionable as disinfectants in pharmaceutical preparations, inhibit the development of germs in very weak solutions, and acid solutions sterilize more easily than do neutral or slightly alkaline solutions.

Iodine is one of the most effective of disinfectants, and preparations containing free iodine in material proportions become sterile of themselves. The same is true of solutions containing chlorine or hypochlorites, or of bromine. The chlorides, bromides, and iodides, in general, have only very feeble disinfecting power, but the soluble fluorides are active.

The salts of mercury and of silver are active germicides and are among the most important disinfectants for physiological use, but they have specific actions which limit, or may prohibit, their addition to pharmaceuticals for antiseptic or disinfectant purposes.

Salts of copper are powerful fungicides, acting in solutions as weak as one part of copper sulphate in one million, but are feeble antiseptics.

Some tellurium compounds have recently been found to possess high bactericidal powers, particularly tellurium-beta-di-ketone. This kills some bacteria in dilutions as high as 1 to 10,000,000 to 1 to 40,000,000. It is toxic, and its bactericidal powers are reduced by blood serum, in which it is efficient in dilutions of 1 to 1,000,000 to 1 to 20,000,000. It is particularly effective in the presence of urine, and has been employed in cystitis and in eye affections.

Other neutral salts are feebly antiseptic and not generally of value for this purpose.

Peroxides, when under conditions by which they liberate nascent oxygen, may sterilize, but are useful only in proportion to their own decomposition. Their antiseptic action is slow and uncertain.

Similar powers are attributed to persulphates and permanganates, which act by liberating nascent oxygen, and which require an intimate contact with the substance to be sterilized to be effective.

Of the organic bodies, alcohol stands first in pharmacy as a preservative.

Alcohol when present to the extent of 18 to 40 per cent is an efficient antiseptic. Solutions containing 40 to 70 per cent are actively disinfectant, the latter strength being most efficient. Above 70 per cent its efficiency tends to diminish, and strong alcohol may preserve, without killing germs.

Formaldehyde is one of the most efficient of disinfectants, and is antiseptic in very small proportions, but may be objectionable for pharmaceutical preparations.

Chloroform, bromoform and iodoform are good antiseptics but are feeble germicides. Chloroform water is a convenient antiseptic for the temporary preservation of drug infusions, or similar preparations, and the chloroform is readily driven out by heat, when desired. Chloramine finds its best use in surgical irrigation. It has been tried internally for intestinal antiseptics but is irritating when used in this way. For external use it is very satisfactory.

Phenol is perhaps the most common of disinfectants, and with tricresol is the most frequent substance used in hypodermic and epidermic medicaments. These have the advantage of combining activity with stability. Other phenolic compounds, as resorcin, thymol, betanaphthol, salol, etc., are useful agents and are frequently used in medication for their antiseptic qualities.

Cresol is three to four times as efficient as an antiseptic as phenol, and is less toxic.

A number of the volatile oils, as anise, clove, cinnamon, pine, wintergreen, etc., possess appreciable value as antiseptics, and while used mainly as flavors are also employed for these other effects.

L. Cavel has reported for each essential oil the minimum quantity that was found necessary to prevent all bacterial growth in ordinary

neutralized meat broth plentifully sprinkled with water from a septic source. The inhibiting quantity of phenol under the same experimental conditions being 5.0 parts per 1,000, the author obtained the following classification for the essential oils:

Thyme 0.7 part per 1,000	Wild thyme 4.0
Marjoram 1.0	Birch 4.8
Orange-peel 1.2	Anise, 4.2
Verbena 1.6	Mustard 4.2
Cassia 1.7	Rosemary 4.3
Rose 1.8	Neroli 4.75
Clove 2.0	Lavender 5
Eucalyptus 2.25	Ylang-ylang 5.6
Mint 2.5	Juniper 6.0
Geranium (Rose de France) 2.5	Fennel 6.5
Vetiver 2.7	Lemon 7.0
Bitter Almond 2.8	Cajeput 7.2
Gaultheria 3.0	Sassafras 7.5
Geranium (Indian) 3.1	Heliotrope 8.0
Spike Lavender 3.5	Cedrat 8.4
Iris 3.8	Turpentine 8.6
Cinnamon 4.0	Camphor 10.0

Seven months after inoculation the culture plates were still sterile when the above quantities were used. These figures must not be taken as absolute, since volatile oils are particularly variable in their antiseptic action as reported. This is probably due to the fact that many oils oxidize easily, and oxidized terpenes, aldehydes and alcohols have a higher antiseptic value than the natural oils.

Benzoic and salicylic acids are often preferred for internal administration. They are efficient as antiseptics, but are feeble as disinfectants.

In foods these are limited to one part per thousand by the food commissioners, which is not sufficient for sterilization but which inhibits the development of most germs.

In selecting an agent for use in medicinal substances it is desirable that the prescriber should be consulted in all cases, when possible, both as to the agent to be used and as to its quantity.

If the responsibility is thrown upon the pharmacist, the first consideration should be the character of the substance to be sterilized, the presence of antiseptic ingredients, whether active or feeble, being considered, and the action of heat upon it. Heat sterilization should always receive first consideration.

If pasteurization only is allowable, the use of 0.5 per cent to 1 per cent of phenol will aid materially in insuring sterility, since all germicides are much more efficient at high than at low temperatures. Tricresol in 0.1 to 0.4 per cent solution is also frequently used. These proportions may not be sufficient in themselves to produce sterility, but they are aids in securing and maintaining this condition, and are usually preferred in preparations for hypodermatic and epidermatic medication.

For medicines for internal administration hydrogen peroxide, sulphurous, salicylic or benzoic acids should be first considered.

One part per thousand is the common limit for these, excepting hydrogen peroxide.

The latter is often efficient in very small proportions (1 in 10,000), but is slow in action, and of little value in mixtures for preserving preparations used intermittently. It has the advantage of not disturbing digestion in any quantity.

Mr. L. F. Gabel carried out a series of tests on thirteen of the more common preservatives, testing each in acid, neutral and alkaline media. He found benzoic acid, salicylic acid, glycerin, alcohol and formaldehyde to be the most satisfactory preservatives for pharmaceutical preparations. (Phenol and phenolic compounds were not tried because the purpose of these tests was to determine the best preservatives for internal use.) Benzoic acid in 0.1 per cent strength and salicylic acid in 0.2 per cent strength were effective against fermentation but not against moulds. Neither was effective in alkaline solution. Glycerin is effective in strength of 45 per cent, but will not prevent mould even in this strength. Alcohol is satisfactory for both ferments and moulds above 15 per cent but alkaline solutions require more than this. Formaldehyde proved to be the most powerful of all substances tried, preventing both moulds and fermentation in acid, neutral or alkaline media in a strength of 0.05 per cent. This is equivalent to about 4 minims of formaldehyde solution per pint, but its use internally even in this strength is objectionable.

Mr. Gabel found chloroform, sulphurous acid, sodium bisulphite, sodium benzoate and sodium salicylate to be inferior as preservatives in the media tried.

The use of chemical disinfectants or antiseptics calls for judgment and some knowledge of the principles involved. No definite proportions can be recommended which will fit all cases. Success in sterilization must depend, as in other things, upon an intelligent application of principles rather than upon a literal following of arbitrary rules.

Surgical antiseptics, in which the antiseptic agents come in contact with the body tissues, presents a special problem. The ideal antiseptic for this purpose is one which will kill microorganisms without harming the tissues of the body;—a condition not easily found when it is considered that an antiseptic is necessarily toxic.

Another factor is that many of the bacterial cells are protected by colloidal lipoids so that aqueous solutions cannot easily penetrate the surface and get at the living germ. Protein matter also hinders penetration and further protects the bacteria. The efficiency of a surgical antiseptic therefore depends not only upon its power over the bacteria but quite as much upon its penetrating qualities and its freedom from harm to the tissues.

The hypochlorites of calcium, sodium and potassium are alkaline in reaction, hence they do not coagulate albumin and they can penetrate the bacteria. They are also non-irritant and practically non-poisonous, and they can dissolve dead tissues. Furthermore they have an oxidizing action and thus destroy toxins which have already been formed, so causing constitutional symptoms to disappear for the time. They are thus well adapted to disinfect open wounds, sores, etc.

Hypochlorites in solution kill most pyogenic organisms in serum at concentrations of 1 in 1,500. Blood decomposes them, however, so that a concentration of 1 in 300 is needed in some cases. They are

used in the form of solution of sodium hypochlorite and the surgical solution of chlorinated soda, or Dakin's solution.

Chloramine acts similarly but is about four times as efficient in equi-molecular proportions. It disinfects very rapidly and the maximum effect is usually obtained in a very few minutes. It is commonly used in 1 per cent or 2 per cent solution, or as a 5 per cent gauze. Ointments of chloramine are practically inert.

Hydrogen peroxide is useful to clear up pus and cleanse wounds or sores, but is not very efficient as a germicide.

Potassium permanganate is useful for irrigation and is mildly germicidal when no serum or pus is present.

Boric acid and perborates are not germicides but they prevent the growth of bacteria.

Iodine in alcoholic solution is very active and is excellent for skin disinfection, but is irritant to wounds.

Iodoform probably owes its entire antiseptic value to the liberation of iodine, and this is a variable process. It has no germicidal properties in itself.

Formaldehyde is too slow in action to be satisfactory for surgical use, and besides it is irritating.

Some of the dyes are of particular value in surgical antiseptics. Their especial advantage lies in the fact that they do not coagulate blood and are compatible with blood serum. They enhance the normal action of blood serum instead of reducing it, and they do not cause irritation. Their disadvantage lies in their being more specific in action than most antiseptics; *i. e.*,—a specific dye may act powerfully upon some germs and be almost without action upon other kinds. They also stain the skin or the secretions with which they come in contact.

The Acridine series, including **Proflavine**, **Trypoflavine**, **Acridine** and **Rivanol** act powerfully upon gonococci and staphylococci in dilutions as high as 1 in 200,000, upon bacillus coli in dilutions of 1 in 100,000, and upon typhosus and anthrax germs in dilutions of 1 in 2,000. The latter strength does not hinder the healing of wounds and is therefore of especial value in surgical treatments.

Sensitol Red represents the Cyanine series and is particularly active upon *streptococcus pyogenes aureus*, killing it in dilutions as high as 1 in 400,000. This has a very feeble action upon *b. coli*.

The Azo dyes are typified by **Trypan Red**, **Trypan Blue**, **Sudan III**, **Scarlet Red** and **Bieberich Scarlet**. These are of especial value in trypanosomiasis (African sleeping sickness) and in promoting granulations in surface wounds, thus hastening healing. The above scarlet dyes are therefore used in ointment or lotion form.

Malachite Green, **Crystal Violet** and **Auramine** represent the Phenyl-methane series and are used in dental and general surgical practice.

Methylene Blue is of the Thiazine series, and has long been used internally in the treatment of local suppuration. It has special action upon staphylococci.

Germ-proof filters are used for liquids, particularly for such as may be injured by heat. Most biological products like serums, vaccines, etc., are sterilized by this means. The filters are made of unglazed

porcelain and act very slowly even when used with pressure. The pores of the filter must be smaller than the germs which they are to exclude, and this means that the porcelain must be thick enough as well as dense enough. They are usually made in the form of a cylinder or bougie and enclosed in an outer cylinder into which the liquid to be filtered is placed, the liquid thus passing from the outside to the inside of the filtering bougie. When properly made they are effective but filter very slowly. Filters of this type which act rapidly should be looked upon with suspicion, because many of them are not germ proof. The filters themselves are sterilized before using by heat, and must be used under aseptic conditions.

The articles which the pharmacist may be called upon to sterilize are injections, gargles, collyria, infusions and decoctions, ointments, dusting powders, etc., and it may be drainage tubes, catgut, gauzes, or surgical instruments.

To most of these heat is applicable, bearing in mind that it must not be employed when it will injure the article.

Powders of all kinds, if not volatilized or decomposed, are best sterilized by dry heat, at a temperature of 150–170° C.

Talcum, kaolin, boric acid, calomel, zinc oxide, and most powders thus used can be sterilized in this way. It has been suggested that iodoform may be sterilized by first moistening with distilled water, then heating in a steam bath for an hour, and finally dried. But one wonders why iodoform, itself an antiseptic, needs to be sterilized at all.

Infusions and decoctions are sterilized in the making, but when strained they are recontaminated, unless the straining is done through sterile gauze or cotton into a sterile funnel and into a sterile bottle, and even then there is great chance of contamination from the air. Fractional sterilization, the heating for 30 minutes on three successive days, is the best method. So prepared they will keep for some days. In fact sterilization is not likely to be demanded for these except for storage purposes.

The Proprietary Association found that for the preservation of vegetable preparations, such as cold infusions, diluted tinctures, fluid extracts etc., not less than 13 per cent of alcohol must be present in bottles which remain unopened, and 17 to 19 per cent is necessary in the case of bottles which are opened and the contents removed in portions. The degree of acidity of alkalinity is also a factor. The more strongly acid the liquid the more resistant it will be to bacterial change. If alkaline it is much more easily attacked. The presence of buffer salts in mixtures, such as citrates, soluble phosphates, amino-salts etc. also make it more difficult to preserve.

Ointments are more apt to be demanded in a sterile condition. Some dermatologists are very particular about this. The easiest method is to sterilize the vehicles and medicinal agents separately, and then make the ointments under antiseptic conditions. Lard, petrolatum, wool fat, glycerin etc., may be sterilized by heating to 120° C. for two hours. If kept in the same jar in which they were sterilized, well covered, and removed as wanted with a sterile spatula, they will remain sterile for weeks. If the active medicinal agent is in itself a germicide, as phenol, iodoform, etc., it may be simply mixed with the vehicle on a sterile slab. Other substances must be treated

according to their character, *i. e.*, sterilized by dry or by moist heat, or by an antiseptic agent. Frequently it will be found that the use of a sterilized vehicle, and the preparation of the ointment under aseptic conditions is all the physician desires.

So prepared an ointment is not strictly sterile, but it is free from pathogenic organisms, and that may be the chief consideration. When ointments are to be applied to a raw or abraded surface, more care is necessary than when they are applied to the unbroken skin.

If it is desired to stir a sterilized ointment while cooling, a rod or spatula should be thrust through a cover of cotton and sterilized with the ointment, then the stirring is performed without removing the cotton.

Injections, particularly hypodermic solutions, are the most delicate class of preparations to sterilize. They consist of potent remedies, in a concentrated form, and frequently they are sensitive to heat. Of the alkaloids, salts of morphine, quinine, emetine, eucaine, strychnine and codeine, will bear the heat of steam for thirty minutes without injury. Solutions of these can be sterilized by boiling, or in the steam sterilizer. Atropine, hyoscyamine, cocaine, eserine, pilocarpine, apomorphine salts and ergot are easily injured by heat, but can be sterilized at 100° C., except eserine, if kept faintly acid. It has been recommended to sterilize them fractionally by heating to 60° C. for thirty minutes on three successive days. This, however, is seldom practicable, on account of the delay. The use of a germ-proof filter is an advantage and when this is not available the containers should be sterilized and sterile water used in making the solution. Recourse may be had to some germicidal agent, and phenol (3 per cent), salicylic acid (1 to 1000), peroxide of hydrogen, formaldehyde, (1 to 5000), thymol (saturated solution), and even corrosive sublimate have separately been suggested. A mixture of salicylic and boric acids has also been recommended as more efficacious than either alone, but it sometimes precipitates the alkaloids when either acid alone would not.

Salicylic acid, formaldehyde, and corrosive sublimate may be objected to, although some physicians might prefer one of them. Phenol is generally considered unobjectionable, and is effective in two and a half per cent solution (or 12 grains to the fluidounce). An effective way of using it, for a cocaine injection, for instance, is to weigh the cocaine and put it into a clean, preferably sterile, bottle. Now drop upon it about one and a half minims of liquefied (95 per cent) phenol, for each fluidrachm of solution, stopper the bottle, and flow it about on the cocaine salt and the whole interior of the bottle. If the phenol does not moisten the entire surface of the glass, add an equal volume of distilled water, and flow as before. Now set the bottle aside for half an hour, and sterilize a sufficient quantity of distilled water by boiling for fifteen minutes. At the end of half an hour the phenol will have sterilized the cocaine and the interior of the bottle and stopper, and the proper quantity of the sterilized water may be poured in and the solution finished by agitation. The graduate in which the water is measured should be boiled twenty minutes, before measuring the sterile water.

Hypodermic injections of most of the sensitive medicaments can be made sterile after this plan.

In some instances the process can be hastened by combining heat (50° to 60° C.) with the germicidal agent, since all germicides act more powerfully in warm or hot liquids.

Thus the preliminary operation may be as before, but after five or ten minutes' action of the phenol, the water may be added at a temperature of 50 to 60° C. (not higher) and this temperature maintained for 30 minutes.

New bottles sometimes give trouble in alkaloidal solutions by causing precipitation. This is due to a slight alkalinity of the glass which dissolves slowly in the water and then reacts with the alkaloid solution. To insure against this it is advisable to rinse the bottle with a hot dilute acid before using, or to acidulate the water used with a slight trace of acetic or tartaric acid. But do not make a decidedly acid solution.

It should also be remembered that new bottles and glassware are hard to sterilize because they are infected to a high degree with the spore of the hay bacillus from the straw in which they were packed for shipment.

Surgical instruments, rubber drainage tubes, etc., are best sterilized by boiling. Wrap all delicate parts and cutting edges in absorbent cotton, place in a towel and make into a compact bundle with a strip of roller bandage, then boil 30 minutes. Surgical knives and sharp cutting tools are boiled only 5 minutes because a longer boiling destroys the edge. One per cent of sodium bicarbonate, or better of borax, should be added to the water in which these are sterilized to prevent rusting. Borax is said to leave steel instruments in better condition than sodium bicarbonate.

The towel and cotton must not be removed until the instruments are used, since they will become reinfected and unsafe to use for an operation if touched or exposed to the air and dust. If the package is to be sent out, wrap it in paraffined paper after draining, and let the surgeon or nurse remove the towel.

Gauzes and dressings are best sterilized in steam, to avoid the possibility of charring and weakening that may occur in a high dry heat. If sterilized by dry heat, the temperature must be watched carefully. Formaldehyde is preferred for rubber articles.

Catgut.—According to Dr. Chas. Rice, the best smooth musical strings may be selected. The best are the violin D, A and E and the first and second banjo strings. These are coated with oil, which prevents their sterilization by alcoholic or aqueous solutions unless the oil is first removed. Three methods are suggested:

1. Simple maceration for at least 48 hours in chloroform saturated with biniodide of mercury. The strings are left in the solution, and taken out when wanted.
2. Boil the strings in enough strong alcohol to cover them, for one hour. The boiling should be performed in a flask provided with a reflex condenser. Then transfer to and keep in chloroform containing biniodide of mercury.
3. Macerate for a few hours in oil of juniper, then treat as in 2.

The second method is more certain than the first, and the third produces a better appearing catgut.

Catgut may also be sterilized by dry heat, provided it is wrapped in paraffined paper and the temperature be raised gradually. A sudden heat makes the gut brittle. Prof. Tscherning's method is as follows: The catgut is placed between sheets of parchment paper in the sterilizing oven and heated for one hour to $60^{\circ}\text{C}.$, then the temperature is slowly raised to $100^{\circ}\text{C}.$, which is continued for two hours, and finally to $140^{\circ}\text{C}.$ for three hours. The gut is then wrapped in the parchment and put into envelopes of parchment paper, which are again heated to $140^{\circ}\text{C}.$ for two hours. These are not opened until required for use.

GENERAL SUGGESTIONS

It must be assumed that every variety of bacteria are present, and that containers, the hands, dust, water, and all substances contain them.

Sterilization should be performed in a place as free from dust and air currents as possible. Bacteria are not found in the air except when the air and the dust are stirred up.

When sterilizing a liquid in a bottle, if a water-bath is used, suspend the bottle in the water clear up to the rim, so that the entire bottle and contents will be thoroughly heated. The stopper should be loose until the liquid has become hot, then it should be pressed in firmly. Use only rubber stoppers in this way.

If corks must be used, stopper the bottle with cotton and submerge the stopper in a solution of bichloride of mercury, 1 to 500. When the liquid is sterile, take up the stopper with sterile pincers (sterilize the tips by heating in the flame), rinse the stopper well with sterile water, remove the cotton from the neck of the bottle, and quickly insert the stopper. Never sterilize corks by heat. Glass stoppers are not tight enough to be trusted.

In sterilizing fluids containing volatile substances, the bottle should be stoppered tightly as soon as it is hot. Very volatile liquids, as ether, chloroform, etc., are sterile in themselves and may be added last.

In fractional sterilization, do not open the bottle after the first heating.

If it is necessary to filter a sterile liquid, the funnel and filter-paper should be first sterilized, and the funnel kept covered during filtration. Filtration should be performed before sterilizing whenever possible.

If an accident occurs, or there is any doubt as to the sterility of a body, sterilize again and be sure of it.

Domestic disinfection is something the pharmacist is frequently consulted about. The popular idea of disinfection is quite a different thing from the scientific idea. True disinfection is a matter requiring intelligent discrimination and some degree of skill. It requires the use of materials in liberal quantities and thoroughly applied. It may be noticed that this is never applied by the householders, but by the agents of the city or town Boards of Health, under whose direction they are used. Laws regulate true disinfection in a way that takes it out of the householder's hands.

The common idea of a disinfectant is more properly a deodorizer. A substance may be a good deodorant but a feeble disinfectant. Yet deodorizing may be valuable, as a preventer of disease. It is a good sanitary measure, at least, and is to be encouraged, aside from its business value.

The most effective deodorants are quicklime, chlorinated lime, sulphate of copper, sulphate of iron and formalin. Three are true disinfectants, for they destroy the germs as well as neutralize the odors. The sulphates are weak as disinfectants, but good as deodorants. Formalin is good in both ways, it sterilizes thoroughly and forms odorless products, but it is expensive. For circumscribed and limited uses it is to be recommended. Quicklime, used as a whitewash, is particularly adapted to sheds, cellars, and musty places. The sulphates of iron and of copper are useful in vaults, etc., as deodorants. Chlorinated lime is useful in outhouses and various places.

Bear in mind that to be really effective **these must come in actual contact** with the surface to be deodorized or disinfected. Simply setting a dish of one of them in the middle of the room will do no good.

Another and more popular class of "disinfectants" are those which are odorous in themselves. These meet the popular idea better than those which are in themselves odorless. Compound cresol solution and the cresylic solutions which dilute to make a milky liquid, etc. are among the most efficient of these. Like the first they accomplish good results when brought into actual contact with the body to be disinfected, but are of little value as gaseous disinfectants. The only really effective gaseous disinfectants are formaldehyde gas, generated fresh and used moist, and sulphur dioxide, also fresh and moist. When these are used in suitable quantities nothing can remain alive in their presence.

Of very little value as disinfectants are the odorous solutions composed of solutions of volatile oils, camphor, thymol, etc. These are good antiseptics when applied in strong enough solution, but when diluted they are feeble. They are popular as deodorants, and they cover other odors.

When a true disinfectant is to be recommended for use in the household, formaldehyde will serve a greater variety of purposes than any other substance. It is cleanly, leaves no traces behind, and it will do as effective work as any. It should be employed in five per cent aqueous solution, and articles to be disinfected must be thoroughly wetted with this, and kept wet for an hour. It does not injure fabrics or colors, and it can be applied to anything, but it makes leather brittle and so is objectionable for furs, book-bindings, etc. Clothing, carpets, furniture, toilet articles, pictures, instruments, fruits, roots, etc., may be thoroughly disinfected by a five per cent. solution of formaldehyde, without injury.

Other agents, as lime, chlorinated lime, phenol, cresol and preparations (compound solution of cresol) are cheaper, and may be used more freely. They are better adapted for outhouses, cellars, walls, and articles that can be easily washed. Lime should be used as fresh milk of lime. Chlorinated lime is best applied in a liquid form, in the proportion of six ounces to a gallon of water. Phenol should be in 5 per cent solution. Compound solution of cresol should be in 2 per cent.

solution. When liquids are to be disinfected, the above strengths should be doubled, so that when mixed with the liquid the strength of the disinfectant will be sufficient. For instance, a 5 per cent solution of phenol is needed for thorough work, but if a 5 per cent solution is mixed with an equal bulk of a liquid to be disinfected, the strength of the mixture will be only two and a half per cent, which is not strong enough to do the work well.

Potassium permanganate is effective as a deodorant, when it comes in actual contact with the decaying body, but it is feeble as a disinfectant. It is more expensive and less cleanly than the other agents mentioned.

Ozonized turpentine, chlorides and other semi-secret or proprietary preparations possess no mysterious advantages, and are easily replaced. For real effectiveness, the manner in which an article is used is quite as important as the article itself.

CHAPTER XVI

BIOLOGICAL PRODUCTS

(Written by L. T. Clark, B. S.)

Antitoxin. Blood serum from an animal which has been immunized with an exo-, extracellular toxin. It may be either the blood serum in its native form or a concentrated and refined product.

Antibacterial Serum. This term is applied to a comparatively large list of serums from animals immunized by the injection of killed, attenuated, or living bacterial cells containing their endotoxins.

Antibody Solution. A modified and dilute form of immune blood serum from which the non-specific protein has been removed.

Aggressins. By-products of bacterial growth developed in the tissues of the animal body or in a medium rich in animal tissue which, on injection as prophylactic agents, produce lasting immunity.

Bacterial Vaccine. A suspension of dead bacterial cells in physiological salt solution. The bacteria may be killed by heat or by shaking with a suitable germicide.

Diagnostic Agents. Antigens, normal and immune serums, and suspensions of killed bacteria for use in the clinical laboratory and at the bedside as aids in diagnosis.

Ecto-antigen. An immune body producing substance which is obtained from the zone of medium immediately surrounding the bacterial cell.

Hemostatic Agents. Serum products to stop hemorrhage by supplying

certain elements which are lacking in blood of abnormally slow coagulation periods.

Modified Bacterial Products. Antigenic substances derived from the bacterial cell, but differing from bacterial vaccines through modifications in the methods of preparation.

Pollen Extract. A specific nitrogenous substance obtained by extracting pollen grains with water, weak alkaline solution or glycerin.

Protein Extract. The specific protein extracted from foods, pollen, epidermal substances, bacteria, condiments, blood serum, etc.

Toxin. A specific substance of bacterial origin possessing highly poisonous qualities but of unknown chemical structure.

(a) *Exo*—extracellular—elaborated in the tissues or medium surrounding the bacterial cell

(b) *Endo*—intracellular—existing within the bacterial cell and less poisonous.

Tuberculins. Products of the growth of the tubercle bacillus in artificial culture media. They are *extractive*, containing the soluble elements of growth, and *residual*, consisting of washed and disintegrated bacilli.

Vaccine. A modified virus which owes its activity to a living principle in an attenuated or weakened form.

This chapter deals primarily with products of bacterial origin. Through popular usage, however, the term Biological Products is now applied to a large list of agents employed in the diagnosis and prophylactic and curative treatment of disease, some of which are not derived from bacteria or their by-products.

With few exceptions, these products are administered by intradermal, subcutaneous, intramuscular, intravenous and intraspinal injection. Such methods of use obviously demand products prepared under most exacting supervision, in sanitary surroundings, to insure purity and freedom from toxic substances and bacterial contamination.

As a means of safeguarding the public against biological products of inferior quality, the Surgeon General of the U. S. Public Health Service is vested with authority by the Treasury Department to inspect and license all establishments engaged in the manufacture of biological products which enter into interstate traffic. This supervision takes the form of periodical inspection of premises and processes, and the examination of products by qualified officials of the Hygienic Laboratory staff. Licenses are granted to cover each individual product offered for sale, only after the U. S. Government officials are satisfied that the product conforms to exacting Government standards.

These standards apply to potency, activity, kind and amount of preservatives, freedom from contaminating micro-organisms or other injurious substances, and to statements on the labels and literature pertaining to the contents of packages, and claims as to what each particular agent may be expected to accomplish in the diagnosis, prevention or cure of disease.

The manufacture and distribution of those biological products intended for the diagnosis or prophylactic and curative treatment of diseases of domestic animals, is controlled in a similar manner by the U. S. Department of Agriculture through the division of Virus and Serum Control of the Bureau of Animal Industry.

Governmental supervision does not apply to all so-called biological products. A limited group of products resulting from bacteriological and mycological researches are now available for use in the arts and industries.

Practically all **Biological Products are of a perishable nature and require a date legend on the package** to indicate the length of time that the contents will be expected to retain their labelled strength under specified conditions of storage. This dating does not mean that the product is of no value after the specified date, because loss of potency or activity is usually gradual. It simply limits the time during which the manufacturer is willing to **guarantee** the strength of the product.

Proper storage of Biological Products is becoming more extensively recognized as of great importance. Definite Government regulations exist which require statements on the labelled packages governing the temperature range under which each product should be kept to insure against undue rate of deterioration. Specially designed cold storage boxes and cabinets are available for such perishable products. Even legislative measures have been passed in certain States making it compulsory to store biological products at a certain range of temperature.

Another important requirement necessary to insure the purity of these agents for injection is their freedom from living bacteria. Because of the unstable character of their protein content, heat may not be employed to a degree sufficient to effect complete sterilization.

Preservatives.—It is customary to add a preservative to biological products to reduce the danger of contamination while in the market or in use. The nature of the preservative depends upon the character of the product and the purpose for which it is intended. As before stated they are used in limited amounts, and for antiseptic rather than for germicidal effect. These agents are therefore to be regarded as aids to preservation and not as complete preservatives.

The percentage of chemical preservatives is also limited, because of the cumulative injurious effect on the product itself and the irritating action of the preservative following injection. Limitations in the matter of preservatives is met by the manufacturer by providing conditions that will afford aseptic technic, thus avoiding contamination rather than to depend on elimination of invading bacteria by strong germicides.

The agents commonly used are glycerin, phenol, trikresol, cresol solutions, chloroform, thymol, and toluol.

The presence of preservatives does not modify the requirements of storage at low temperature.

Datings which manufacturers place on the finished packages are arrived at by repeated activity or potency tests, or by comparison with products of like nature on which a safe time limit has already been established. Data has been accumulated by several manufacturers and by the U. S. Hygienic Laboratory, on which the present datings of the most extensively used Biologicals are based: It is conceded that the loss of potency of the proven Diphtheria and Tetanus Antitoxins is more rapid directly after removal of the serum from the horse than later on during the life of the product.

While it is practically impossible to determine the exact rate of deterioration for the classes of products on which definite measure of potency has not yet been made possible, it is undoubtedly true that they are less potent when the dating expires, but still sufficiently active to accomplish the desired results.

Under the best conditions, deterioration usually takes place gradually, but if kept cold without being frozen, they remain potent much longer than if exposed to ordinary climatic changes.

It cannot be too greatly emphasized that **each biological product, particularly of the serum and vaccine class, deteriorates at a rate peculiar to itself, and requires special care in storage.**

The Veterinary Products do not differ in any essential way from those made for human subjects. They may be specially prepared from species of bacteria which are pathogenic only to animals, or they may be the same as those prepared for man but made of higher strength or supplied in larger doses.

Products for Veterinary use are made under similar supervisional requirements and with the same care as for other biological products, and possess similar keeping properties.

SERUMS

Immunity may be **natural**, due to the resistance of the normal body to disease, or **acquired** due to an invasion of disease or to the introduction of artificially immunizing antigens. Acquired immunity is classed as **active** when it results from a vaccine or from the injection of bacterial products or from disease processes. It is **passive** when it results from the *introduction* of antistances which are antagonistic to the disease toxins, and which are known as antibodies. These antibodies must be developed in the living body by the natural resistance of that body, augmented as the disease continues by the increased formation of antistances. When disease-producing toxins are elaborated in the

body, nature combats them by the formation of specific antibodies or antitoxins which antagonize or neutralize the toxin. Hence if a blood serum in which these antibodies have been formed be introduced into the blood of a person who is threatened with or is suffering from the disease, the resistance of the individual is thereby increased in proportion to the amount of antibodies introduced. Passive immunity is temporary, lasting only as long as the specific antibodies remain in the system.

The kind of immunity to be considered under Serums is therefore passive immunity. It does not last nearly as long as active immunity, but it has the advantage of being induced without delay. Serums are therefore employed either during all stages of the disease, or as a prophylactic after exposure.

Antitoxins

Diphtheria Antitoxin
Tetanus Antitoxin
Scarlet Fever Streptococcus Antitoxin
Erysipelas Streptococcus Antitoxin
Perfringens Antitoxin
Botulinus Antitoxin.

These are the oldest and most efficient of the products intended to convey passive immunity. These contain specific antibodies which act as positive neutralizing substances against the toxins by which the animals used in their production were immunized.

The strength of an antitoxin is expressed as *potency*, which is the basis of its value and may be measured by its neutralizing effect on the toxin of its origin.

Diphtheria Antitoxin.—To prepare this antitoxin, a pure culture of the diphtheria bacteria is first obtained by growing the germs on blood-serum culture medium and separating them from contaminating organisms by proper means. The pure culture is then transferred to a bouillon medium and incubated at a temperature of 37° C. Rapid growth takes place, and during this growth toxins are formed which diffuse throughout the bouillon. After about 2 weeks the germs are removed by filtration through a germ proof filter, leaving the bouillon rich in diphtheria toxin.

This toxin-laden bouillon is then injected into healthy horses, first in very small doses. The toxin produces reactions in the horse similar to the disease, and the blood of the horse resists by forming antibodies. When the effect of the first dose has passed off, a second and larger dose is injected, producing similar results and more antibodies. This process is repeated until the horse will tolerate enormous doses of the toxin without serious reaction. The first dose may be as small as 1 cc. and the last as large as 350 cc. During this period the tissues are constantly forming the antibodies which enable the horse to resist the action of the toxin. When the resistant powers of the horse have been fully developed, which usually requires 2 to 3 months, the animal is allowed to rest 8 to 10 days, during which time all traces of toxin are eliminated from the animal's system.

The horse is then bled from the jugular vein under aseptic conditions, the blood being collected in sterile glass tubes or bottles. After standing 24 to 72 hours the blood clot separates from the serum, and the latter, which contains the antibodies, is poured from the clot. A preservative, 0.4 per cent of trikresol, or 0.5 per cent of phenol, is then added and the serum is stored in a cold chamber maintained at a constant temperature just above freezing.

The potency of each lot of serum is then determined by testing its neutralizing value against diphtheria toxin in the following manner. The test-dose of toxin used in this determination is fixed by the U. S. Government, and is approximately 100 times the amount fatal to a

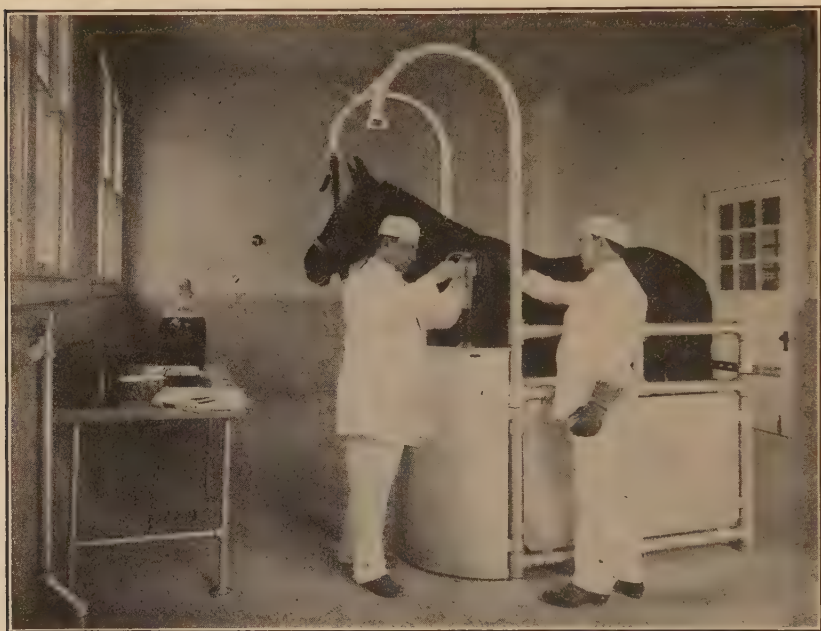


FIG. 75.—Injecting toxin.

250-Gm. guinea-pig. Each of a series of dilutions of the serum to be standardized is mixed with one test-dose (L+ dose) of toxin, and allowed to stand 20 minutes. Each mixture is then injected subcutaneously into a 250-Gm. guinea-pig, and the pigs are kept under observation 4 days. Those animals which die within this period indicate the presence of unneutralized toxin in the mixture injected, while those living at the end of the period show that the test-dose of toxin has been neutralized by that particular dilution of serum. The smallest quantity of the serum which will preserve the life of a 250-Gm. guinea-pig during 4 full days, in the presence of the test-dose of toxin, is called **one antitoxic unit**. Consequently if one-five-hundredth of a cc. of serum under test protects the guinea-pig, that particular serum would be rated as containing 500 antidiphtheric units.

For a number of years after diphtheria antitoxin was originated it was used in the form of native serum,—that is, the serum after being standardized was filtered, tested for sterility and distributed for use as horse serum containing the specific diphtheria antitoxin. It very soon became apparent that the volume of such native serum needed to administer the number of antitoxin units was objectionable on account of introducing the large quantity of foreign protein present in the native serum.

Various methods were attempted to concentrate the serum into smaller volume without loss of units and to eliminate the objectionable albumens and proteins.

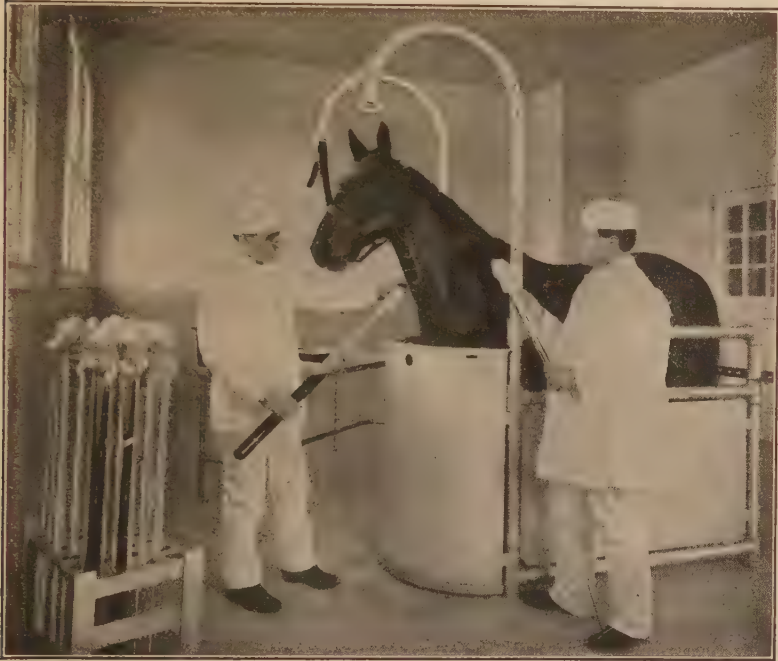


FIG. 76.—Bleeding a horse for antitoxin.

The researches of Peck and Atkinson demonstrated that the antitoxic potency of antidiphtheric serum was associated with the globulins in the serum. Gibson and Banzhaf, working in the Laboratories of the Health Department of New York City, then revealed that the antitoxin units were carried by the pseudoglobulin fraction, and that by precipitation with the proper concentration of ammonium sulphate this antitoxin bearing fraction could be thrown down and the bulk of the non-antitoxic fraction—eu-globulin—eliminated. Numerous modifications of the original methods of Gibson and Banzhaf are now in general use by the manufacturers, making it possible to eliminate a large percentage of the non-essential elements of antitoxic serums, and to effect a concentration approximating one-fourth of the original

volume, with a concurrent increase in the number of units per cc. of the concentrated product.

Since 1905 Diphtheria Antitoxin has been available in a concentrated and refined form, made possible by this process of double precipitation, filtration and dialysis. The antibody, bearing pseudo-globulins, is separated from a large proportion of the inert and non-antitoxic ingredients of natural serum, and represents the potent principle of the commercial antitoxin in the smaller volume. The resulting product is clear, less liable to produce anaphylaxis than native serum and is adjusted to contain not more than 20 per cent. total solids. This maximum limit of total solids is established by U. S. Government regulations and is in accord with U. S. P. specifications.



FIG. 77.—Separating serum from blood clot.

Diphtheria antitoxin is now sold exclusively in the refined and concentrated form. Definite continuous improvements have been accomplished in the concentrating and refining process, by reducing the volume in which a given number of units are represented; it is to be expected that even greater advances in the purification of this important biologic will eventually occur.

The finished product is now made available in syringes and bulbs containing 1000, 3000, 5000, 10,000, 20,000, and 40,000 units, in comparable volumes of liquid ranging from less than 1 cc. to 10 cc.

Tetanus Antitoxin.—For use in both human and veterinary medicine.

The details which apply to the production of tetanus antitoxin are very similar to those given under Diphtheria Antitoxin (page 343).

The principal differences exist in the cultural requirements of the organism and in the potency standard.

In the production of tetanus toxin the bacillus of tetanus (lockjaw) is grown in a nutrient medium under anaerobic conditions, (free from atmospheric oxygen) and carried through the filtering and testing processes in quarters entirely apart from the other laboratories, because of the difficulty with which the tetanus spores are killed. This precaution assures a greater degree of safety from the contamination of other products and glassware with the resistant tetanus spores.

Tetanus antitoxin is also tested on guinea pigs to determine its neutralizing power against the toxin of its origin. Pigs weighing 350 grams are used because of greater susceptibility to tetanus toxin.

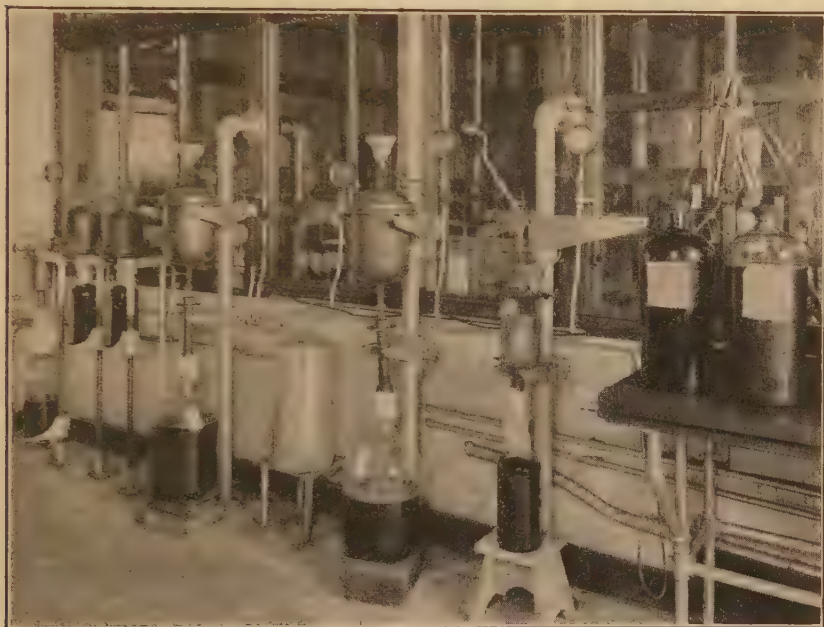


FIG. 78.—Apparatus for filtering antitoxins.

The standard tetanus antitoxin unit is expressed as ten times that quantity of antitoxin necessary to protect the life of a 350 gram guinea-pig for four days in the presence of one U. S. Government test dose of tetanus toxin. The test dose of toxin is approximately 100 M. L. D's, (minimum lethal doses) and the tetanus antitoxin unit is calculated 10 times the quantity necessary to neutralize a test dose of toxin.

While the greater proportion of tetanus antitoxin is concentrated and refined, quantities of the product are still being supplied in the form of unconcentrated native serum, particularly for veterinary use in packages of lower total unitage. The commercial product for use on human beings is supplied most extensively in syringe containers, although it is also furnished in bulbs. For veterinary use a demand occurs also for syringes, bulbs and vials. Containers for human use are

available with 1500, 3000, 5000, 10,000 and 20,000 units in volume ranging from 1 1/2 cc. to 10 cc. The number of units in packages for veterinary use is 500, 1500, 3000, 5000, 10,000, but in a range of volume considerably greater than is to be desired in human medicine.

Scarlet Fever Streptococcus Antitoxin

The streptococcus isolated from scarlet fever and believed to be the cause of this disease produces a filtrable toxin when grown in a liquid nutrient medium. The liquid cultures are incubated at 37° C. for 6 days, and then filtered to remove bacteria. This toxin is injected subcutaneously into horses, in gradually increasing doses, until the blood of the horse contains a maximum content of antitoxic units.

The unit of Scarlet Fever Streptococcus Antitoxin is that amount of serum that will neutralize one skin test dose of scarlet fever streptococcus toxin when injected intracutaneously into the arm of a human being susceptible to scarlet fever. The serum of the average horse, fully immunized to the toxin, contains from 10,000 to 20,000 units per cc.



FIG. 79.—Testing antitoxin.

This serum is also concentrated and refined before being made available for use in the prophylactic and curative treatment of scarlet fever, and is supplied in two strengths, 150,000 neutralizing units for prophylactic effect, and 300,000 neutralizing units for curative results.

The above described method for the preparation of Scarlet Fever Streptococcus Antitoxin was originated by Drs. Geo. H. and Gladys F. Dick. Other methods are also used. The Dochez method involves the introduction of toxin into the horse by impregnating masses of culture medium, deposited beneath the skin, with live cultures of the streptococcus which continue to multiply and provoke a continued absorption of the toxic substances given off by the growing culture. In fact, the horse acts as its own incubator in the development of toxin with which it becomes highly immunized. Serum resulting from this method of immunization is also antitoxic.

Erysipelas Streptococcus Antitoxin

A streptococcus isolated from patients suffering from erysipelas now is believed to be the cause of that disease. Cultures of this organism have been demonstrated to produce a soluble specific toxin when grown in suitable culture media. The antitoxin is prepared by injecting horses with the toxic culture filtrate, the entire liquid culture, suspensions of killed and living organisms, or a combination of these by-products. The serum is tested for potency on human beings by determining its neutralizing power on erysipelas streptococcus toxin.

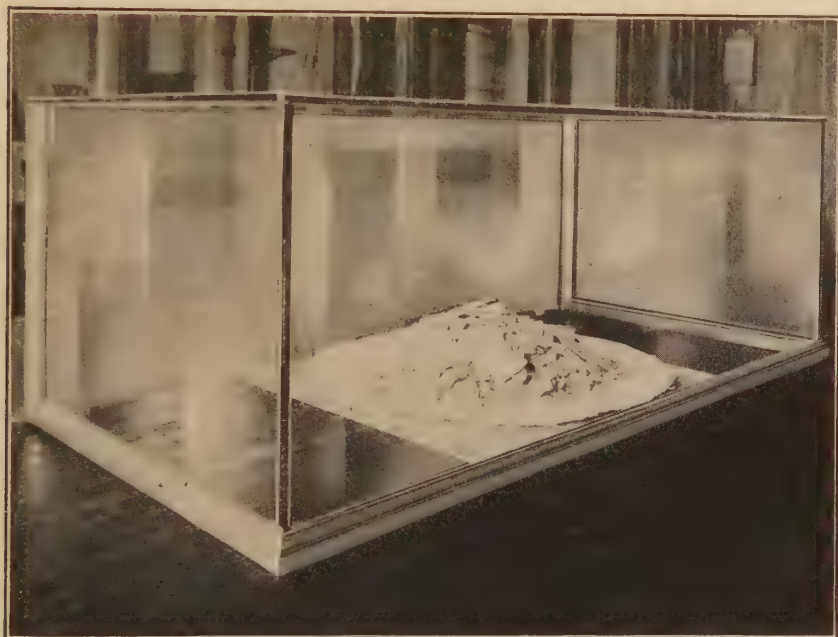


FIG. 80.—Precipitated globulin.

One "unit" arbitrarily taken, but not as yet generally adopted, is that amount of antitoxin required to neutralize one hundred skin test doses of erysipelas streptococcus toxin.

Before the serum is made available to the trade it is reduced to a concentrated and refined (globulin) product and is supplied in 5000 "unit" syringe packages.

Perfringens Antitoxin

This antitoxin is contained in the blood of horses highly immunized with a toxin obtained by growing highly virulent cultures of *B. Welchii* in liquid culture media. The toxin is prepared as a filtrate from these cultures and is rendered germ free by filtration through germ proof filters. After its freedom from the organism is assured by test on culture media, its activity is determined by test in serial dilutions on pigeons and expressed in terms of L+ dose, or that amount of toxin which will kill a pigeon in the presence of 1/100 unit of antitoxin.

The horse is injected subcutaneously at intervals of 3 to 4 days, with gradually increased doses of perfringens toxin, until its serum reaches a definite standard of potency.

The perfringens unit is equal to the amount of perfringens antitoxin contained in one cc. of serum of average high strength, arbitrarily set aside to serve for purposes of comparison.

The most extensive use of Perfringens Antitoxin occurred during the World War, when it was injected, in conjunction with Tetanus Antitoxin, as a prophylactic measure against gas gangrene due to *B. Welchii*. It is usually supplied in containers of approximately 10 cc.

Botulinus Antitoxin.—For human and veterinary use. Within comparatively recent years the relationship between food and forage poisoning and *Bacillus botulinus* has been definitely established. It is also conceded that the symptoms of botulism occur very early after the ingestion of preformed toxins which have developed from the growth of the organism in the food before being taken into the body. Two types of the organism, "A" and "B," are employed in the production of toxin with which horses are immunized.

In the production of the polyvalent antitoxin, the horses receive repeated injections of non-lethal amounts of toxin, obtained from the growth of both "A" and "B" types, grown in suitable culture media. The toxins are standardized as to activity by testing on 250 gram guinea pigs to determine the minimum lethal dose (M. L. D.).

At the completion of the immunization process the blood is drawn in the usual manner, preserved, filtered, and tested for sterility and potency.

A standard unit of potency has been adopted by the Hygienic Laboratory, and may be expressed as that quantity of antitoxin that will just save the life of a 250 gram guinea pig against 1000 M. L. D.'s of the toxin. This test and the expression of unit value of each lot of antitoxin are analogous to the methods used in the standardization of tetanus antitoxin. The antitoxin is tested against both toxins "A" and "B" separately and its potency value so expressed.

Botulinus antitoxin Type "A," and polyvalent types "A" and "B" are now available, for use in human and veterinary medicine, in packages of 40 cc. (8000 units A. & B.) and 200 cc. (40,000 units A & B.). This antitoxin is for both prophylactic and curative treatment of man and animals.

ANTIBACTERIAL SERUMS

FOR HUMAN BEINGS

Antianthrax Serum	Antimeningococcic Serum
Antidysenteric Serum	Antiplague Serum
Antigonococcic Serum	Antipneumococcic Serum
Antimelitensis Serum	Antistreptococcic Serum

FOR VETERINARY USE

Antianthrax Serum	Anti white scour (anti calf scour) Serum
Antiblackleg Serum	Anti hog cholera Serum
Antidistemper Serum (canine)	Anti mixed infection Serum (for swine)
Antihemorrhagic septicemia Serum	Anti pig dysentery Serum
Anti bovine abortion Serum	Anti mixed infection Serum (avian)
Antiinfluenza Serum (equine)	Anti navel ill Serum (equine)
Anti equine abortion Serum	Anti swine erysipelas Serum
Antistreptococcic Serum (equine)	

The greater proportion of pathogenic bacteria do not produce a soluble toxin the strength of which can be measured by methods now available. The toxic elements of members of this group are contained within and are a part of the bacterial cell.

The term **Endotoxin** is therefore applied to those toxic substances which are obtained by the disintegration of bacterial cells, either within the body or from pure cultures by artificial means.

In contrast to the methods which suffice for determining the strength of an antitoxin, the value of an antibacterial serum cannot be definitely determined by its neutralizing power. A number of methods which involve rather delicate technique have been developed which demonstrate that antibacterial serums do possess antibodies. The antibodies in these include agglutinins, opsonins, precipitins, lysins and specific antigen—complement fixing qualities. These substances can be demonstrated in a serum, but there are no practical means for definitely measuring their power other than by comparison with an arbitrary standard serum. Their presence is considered a reliable indication that the process of immunity has been carried to a comparatively high degree in the animal from which the serum is obtained. Thus there is evidence that the antibacterial serums possess potency, but there is no way of measuring that potency with sufficient degree of accuracy to permit of its being expressed in units.

Antianthrax Serum.—For use in both human and veterinary medicine. The production of a specific serum of value in the prophylactic and curative treatment of anthrax is surrounded with some difficulty—because the causative organism, *B. anthracis*, is a very resistant spore former.

The latest methods involve the injection, intravenously, of killed organisms, followed by living suspensions of both vegetative and spore forms; the stimulation thus produced is followed by a rapid accumulation of specific antibodies in the blood of the animal being immunized.

Horses and cattle are usually depended on for commercial production and develop an early tolerance to massive doses of living virulent spore suspensions of the bacillus of anthrax.

The agglutination test has come to be recognized as a dependable means for evaluating the degree of immunity produced in the animal's blood. When sample bleedings show that the serum in dilutions from 1-5000 to 1-10,000 gives complete agglutination (clumping of dead anthrax bacilli) it is of sufficient potency for use.

At least 17 days are allowed to elapse between the last injection and the bleeding, to insure complete elimination of living spores.

The serum is collected, preserved, filtered and tested in the usual manner.

Antianthrax serum is of value in the prophylaxis and therapeutic treatment of anthrax in both human beings and domestic animals. For human practice it is supplied in syringes and vials of 50 cc., while for veterinary use containers of 10 cc. to 100 cc. are furnished. The smaller dosage is employed in conjunction with anthrax vaccine (page 374) for simultaneous prophylactic treatment.

Antiblackleg Serum, Veterinary.—Antibodies are produced in the blood of the horse by repeated injections of pure cultures of *B. chauvæi*, the cause of blackleg, in increasing amounts.

The serum resulting has only a limited use, because of the rapidity of the disease process and the cost involved in the large quantities of serum required to give beneficial results. Its use is practically limited to very valuable registered animals, and to the early stages of the disease.

Antidistemper Serum (Canine), Veterinary.—Efforts to determine the true cause of distemper among dogs have resulted in a division of opinion among the several investigators. One group of workers believe the cause to be an organism called bacillus bronchisepticus, first isolated and named by Dr. N. S. Ferry, which may be isolated during practically all stages of the disease, while another group of investigators maintain that the real cause is a filtrable virus of unknown classification, and that bacillus bronchisepticus is of secondary importance.

The large majority favor bacillus bronchisepticus as the cause of the disease, hence the production of an antibacterial serum for prophylactic and curative treatment is founded on this organism. Culture suspensions are injected into the horse subcutaneously or intravenously, over a sufficient length of time, and in sufficient increased doses to bring about a high degree of immunity in the animal as determined by the agglutination test. When a maximum standard is reached the horse is bled, and the serum is collected and preserved.

No standard of potency is available with which to test the final product other than its content of agglutinins.

The serum is supplied in packages that provide both single and multiple doses of from 5 cc. to 10 cc.

Antidysenteric Serum.—Several types of the dysentery bacillus have been isolated and identified as the cause of bacillary dysentery. These types are recognized as "Shiga," "Flexner" and "Hiss Y" and others, and possess differential qualities which may be detected by cross-agglutination tests.

The "Shiga" and "Flexner" strains of the organism are recognized as of most frequent occurrence in infection, and therefore are taken as the basic strains for serum production. After repeated intravenous injections of the various cultures into the horse, the blood is drawn, the serum collected, preserved and tested for agglutinin content.

An arbitrary standard Antidysenteric Serum is supplied by the Hygienic Laboratory to serve as a control serum. All lots of commercial serum must conform to this standard. Antidysenteric Serum is made available in syringes and bulbs, to provide doses ranging from 10 cc. to 100 cc., for both prophylactic and curative use.

Antigonococcic Serum.—This is usually obtained from horses which have been immunized against either the disintegration products of the diplococcus of gonorrhea, in the form of filtered germ-free autolysates injected subcutaneously, or against intravenous injections of, first, killed, and later live, organisms. When this latter method is employed, the culture mass is removed from the medium immediately before injection, to avoid extensive autolysis.

Progress toward immunity is determined by frequent tests on samples of blood by both the agglutination and complement fixation tests. No Government standard has been placed on this serum; the manufacturer, however, arbitrarily adopts a minimal titre to which the serum from each horse must conform before regular bleedings are taken.

The serum is offered in packages of 2 cc. to 12 cc. and is obtainable in both glass bulbs and syringe containers. It is recognized as of limited value, by subcutaneous or intravenous injection, in the treatment of chronic gonorrhea with arthritic involvement. Antigonococcic serum is not recommended for the treatment of acute gonorrhea.

Antihemorrhagic Septicemia Serum (Veterinary).—Several species of the domestic animals, including horses, mules, cattle, swine, and sheep, are subject to infection with bacterium septicum, which may become enhanced in virulence during the course of an epidemic and cause severely rapid and extensive losses among live stock, particularly during shipment and in stock yards.

An antibacterial serum for both prevention and cure is made possible through the hyperimmunization of horses with polyvalent suspensions of, first, killed, and then living, organisms. During the early development it was believed necessary to prepare a serum by injecting horses separately with strains of the organism from each species of animal susceptible to infection. Fortunately, later cultural study and comparison of strains have demonstrated the absence of differential characteristics in the species strains, and a serum is now prepared that will serve equally well for all species of animals.

Antihemorrhagic septicemia serum is supplied in bulbs and vials of single and multiple doses of 10 cc. to 100 cc.

Antiinfluenza Serum (Equine), and Antistreptococcic Serum (Equine) Veterinary.—These serums are prepared by hyperimmunizing horses against streptococci, both hemolytic and non-hemolytic, found associated with equine influenza and the various streptococcic infections, respectively.

No standards of potency have been adopted. The blood is drawn after the horse has received a maximum number of injections of killed, and later, living organisms, in quantities sufficient to give rise to pronounced thermal reaction after each injection.

The filtered, preserved and tested serum is made available in syringe and vial containers of 10 cc. to 30 cc. to provide for a range in dosage from 10 cc. to 90 cc.

Antimeningococcic Serum.—In the preparation of this serum, polyvalent cultures representing the four groups of the diplococcus of meningitis are injected into horses intravenously. The suspensions for the first injections are usually killed by heat, but the later injections consist of large quantities of the culture mass of living organisms, administered intravenously immediately after removal from the culture medium.

An arbitrary standard of potency has been adopted by the Hygienic Laboratory and is represented by a control standard serum which is furnished each manufacturer. Each lot of commercial serum must conform to this standard, in that test suspensions, representing each of the four groups, must be agglutinated by the serum under test, in dilutions on a par with similar dilutions of the standard serum.

Antimeningococcic Serum is put up in specially designed syringe containers to provide convenient and immediately available means for intraspinal injection. Usually these syringe containers also permit of injection by either the gravity method or by pressure exerted on the plunger, and are of 15 cc. to 50 cc. capacity.

Antiplague Serum.—Produced in horses by the injection of suspensions of the bacillus of bubonic plague. The serum possesses both antitoxic and antibacterial properties, and is made available in suitable containers to provide 20 cc. prophylactic, and 100 cc. treatment doses.

Antipneumococcic Serum.—While four serological types of the pneumococcus are recognized as causing pneumonia, only Type 1 is adapted to the production of an antiserum. Horses receive intravenous injections of large quantities of centrifugalized suspensions of, first, killed, and then living, organisms, from liquid culture media, over sufficient lapse of time to bring about a maximum development of specific antibodies in the horse's blood.

Progress toward antibody production is determined by the mouse protection test, which is the basis for a standard of potency imposed on the manufacturer through Government regulations. A control standard antipneumococcic serum is supplied to each producer, for purpose of comparison, which must give the same degree of protection to mice simultaneously injected with a killing dose of a very virulent culture of pneumococcus Type 1.

Antipneumococcic serum to be of value must be injected early and in relatively large doses, and is usually put up in 50 cc. syringe containers.

Antistreptococcic Serum.—This, the first antibacterial serum to be used for the treatment of disease, still retains an important place in biological medicine, even though no definite methods have been perfected for evaluating its potency in the laboratory.

Antistreptococcic serum is usually polyvalent, in that the strains of the streptococcus used in its production represent both the hemolytic and non-hemolytic varieties of the organism, and are selected from the several classes of infectious processes due to streptococci.

Horses under immunization are given increasing doses of suspensions of the several strains, usually intravenously, sufficient to produce maximum thermal reactions over a period of weeks. After bleeding, the serum is collected, preserved, filtered through germ proof filters, tested for sterility, and filled into both bulb and syringe containers of 10 cc. to 50 cc. capacity.

No standard of potency is as yet available for this antibacterial serum, its value having been proved through extensive clinical use.

Anti White Scour (Anti Calf Scour) Serum (Bovine) Veterinary.—*Bacillus coli*, isolated from cases of white scour in calves, is recognized as the cause of white scour, hence several strains of this organism are used in the production of an antiserum. Horse are hyperimmunized with suspensions of the organism removed from solid culture medium, until their blood serum gives a high agglutinin titre.

The potency of the serum as marketed is not fixed to any definite standard. The serum is supplied in bulbs and vials, which provide both single and multiple doses of 10 cc. to 100 cc.

Anti Hog Cholera Serum Veterinary.—This is undoubtedly the most extensively used antiserum in veterinary practice. It is obtained from hyperimmune hogs which have been immunized to injections of hog cholera virus. The etiological cause of hog cholera has not as yet been determined. The infectious principle is a filtrable virus and may be maintained indefinitely by periodical injections into normal pigs

The serum is marketed in three grades, two clear serums representing advances in precipitation and refinement, and the other, a mixture of serum and hemoglobin. An arbitrary standard of potency has been adapted, which requires that 20 cc. doses must protect 45 lb. to 90 lb. pigs against 2 cc. of controlled virus injected simultaneously.

It is supplied in single and multiple dose packages, to provide economical distribution, of 20 cc. to 75 cc. doses, depending on the size of animals to be treated.

This serum is used alone and in conjunction with hog cholera virus. (See page 377.)

Anti Mixed Infection Serum (for Swine), Anti-pig Dysentery Serum and Anti-swine Erysipelas Serum Veterinary.—These represent a group of antibacterial serums for use in the prophylactic and therapeutic treatment of infectious diseases prevalent among swine, particularly where the pig raising industry is carried out on a large scale. These three serums differ only in the strains used in their manufacture, and are made available in packages suitable to provide serial dosage. No standards of potency are as yet available.

Anti Mixed Infection Serum (Avian) Veterinary.—An antibacterial serum prepared by hyperimmunizing horses with strains of streptococci, *b. pyocyaneus*, *b. coli* and *b. avisepticus* isolated from fowls suffering from mixed infections including roup and fowl cholera.

No standard of potency is available for testing this serum. It is sold in multiple dose packages of 20 cc. to 100 cc. to afford convenient means of withdrawing doses of 2 cc. each.

Anti Navel-ill Serum (Equine) Veterinary.—It is believed by many practitioners that navel-ill (joint-ill) is due to a mixed infection with bacillus coli, streptococci and staphylococci. An antiserum is produced in the horse by repeated injections of suspensions of these organisms. The serum is not standardized for potency and is marketed in containers of 20 cc. and 100 cc. for dosage of 10 cc. to 20 cc.

Early in the development and use of antitoxins and antibacterial serums, a demand occurred in the United States for a syringe container that would facilitate quick, convenient and easy administration, particularly under conditions where ready means for sterilizing a syringe were not available. This demand was met by the manufacturers by supplying these products in the syringe container that is now in popular use. These syringes are of various designs although very similar in their essential principle and provide a comparatively inexpensive, convenient and easily operated container in which the product is adequately protected against contamination. The needle accompanying each syringe container is also so protected in a sterile tube as to permit of being readily assembled with the container without danger of contamination.

While the general use of the syringe container continues, a limited proportion of the serums are being supplied in bulbs and vials for use with standard hypodermic syringes. The reverse is true in other countries where bulb containers are used almost exclusively.

ANTIBODY SOLUTION

As the name implies, this heading refers to a distinctly separate group of biological products, having as its basis those products which

carry the specific antibodies in clear solution, and free from the non-essential fractions of their parent serums, being particularly free from serum proteins.

Pneumococcus antibody solution is prepared by treating suspensions of the three types of the pneumococcus I, II, and III with potent antipneumococcic serum, after which the bacteria are separated from the serum in which they have been bathed, and further manipulated to cause a dissociation of the antibodies from the bacterial cells. The affinity bacterial cells possess toward their homologous antibodies makes it possible to employ the cells merely to pick out the antibodies from the serum, leaving behind those nonessential elements of the serum, including the serum proteins, which possess the objectionable tendency of producing serum sickness and anaphylaxis.

Pneumococcus antibody solution is a clear, isotonic solution, rendered sterile by filtration through germ proof filters. It is available in 50 cc. vials and is recommended to be injected intravenously.

AGGRESSINS—VETERINARY

Anthrax aggressin

Blackleg aggressin

Blackleg filtrate

Hemorrhagic septicemia aggressin

During the course of the disease process, following infection with certain highly virulent microorganisms pathogenic to domestic animals, a specific protective substance is formed in the liquids which accumulate within and intimately adjacent to the infected areas of the body. This protective quality develops as a result of the antagonistic reaction of the body cells against the invading bacteria and is called natural aggressin. In the late stages of the disease this serous exudate accumulates in appreciable quantities in the connective tissue, muscle tissue, and viscera of the affected areas.

Similar results are obtained in quantity production of natural aggressin by infecting susceptible animals with virulent strains for each specific aggressin. Directly after death, this exudate, rich in aggressin, is collected by extracting the dissected tissue under pressure into sterile containers. A suitable preservative is immediately added, and the sediment is then removed by filtration through germ proof filters. The clear, sterile, serum-like fluid is subsequently filled into sterile containers of various sizes, to provide multiple dose packages for convenience in administration.

This method of production of natural aggressin applies to the preparation of Anthrax, Blackleg and Hemorrhagic septicemia aggressins.

Artificial culture Aggressin (Blackleg filtrate) is obtained from the growth of the organism in a culture medium containing an abundance of animal tissue, in large flasks which are incubated at body temperature. After incubation a preservative is added, and the fully developed cultures are filtered through germ proof filters resulting in a clear germ free filtrate. This filtrate is equally as active as natural aggressin as an immunizing agent and is supplied in similar packages.

Aggressins are used exclusively in veterinary practice, usually in 5 cc. doses and only for the preventive active immunization of susceptible animals against infection. No standards of activity have been adopted for these products.

BACTERIAL VACCINES (BACTERINS)

Owing to the very large number of bacterial vaccines representing a single species and various combinations of species, to the numerous trade names which are applied to similar combinations, or combinations differing only in bacterial count, and to the frequent changes which are made in bacterial content and species combinations, no attempt will be made here to list each individual vaccine now available.



FIG. 81.—Making bacterial vaccines.

The following list includes all the species of organisms that may enter into the production of bacterial vaccines, either singly or in combination, under U. S. Government license for use on human beings. The products are therefore referred to as

Bacterial Vaccines made from:

acne bacillus
acne diplococcus
cholera vibrio
colon bacillus
dysentery bacillus
enterococcus
Friedlander bacillus
gonococcus
influenza bacillus
meningococcus
micrococcus catarrhalis
micrococcus melitensis
micrococcus tetragenus

nonvirulent tubercle bacillus
paratyphoid bacillus A
paratyphoid bacillus B
pertussis bacillus
plague bacillus
pneumococcus
prodigious bacillus
pseudodiphtheria bacillus
staphylococcus albus
staphylococcus aureus
staphylococcus citreus
streptococcus
synococcus

typhoid bacillus.

Under license by the Bureau of Animal Industry, for use in veterinary practice, the following list includes representative products. The Bureau of Animal Industry makes a distinction between "Vaccine" and "Bacterin" as the terms are used on labels. The term "Vaccine" is to indicate that the organisms, contained in the product, are in a living and attenuated form, while "Bacterin" signifies that the organisms have been killed during the manufacturing process.

Autogenous bacterin	Gastroenteritis mixed bacterin (equine)
Abortion bacterin (equine)	Hemorrhagic septicemia bacterin
Abortion bacterin (bovine)	Hemorrhagic septicemia and infectious enteritis mixed bacterin (swine)
Abortion bacterin mixed (bovine)	Infectious rhinitis mixed bacterin (for swine)
Abortion bacterin mixed (equine)	Keratitis mixed bacterin, bovine
Abortion bacterin mixed (swine)	Mastitis mixed bacterin (bovine)
Blackleg bacterin	Metritis mixed bacterin (bovine)
Bacillus suispestifer bacterin	Mixed infection bacterin (avian)
Canine distemper antigen	Mixed infection bacterin (bovine)
Canine distemper bacterin	Mixed infection bacterin (canine)
Canine distemper mixed bacterin	Mixed infection bacterin (equine)
Colon bacterin (equine)	Mixed infection bacterin (bovine)
Colon bacterin (bovine)	Mixed infection bacterin (porcine)
Calf scour mixed bacterin	Mixed bacterin (for rabbits)
Distemper mixed bacterin for horses	Navel ill mixed bacterin
Equine influenza bacterin	Pneumonia mixed bacterin (equine)
Equine influenza mixed bacterin	Pig scour bacterin
Equine staphylococcus aureus and albus bacterin	Staphylo bacterin (goats, equine, canine)
Endometritis mixed bacterin, (bovine and equine)	Strepto bacterin (canine)
Fowl cholera bacterin	Streptococcus mastitis bacterin (bovine)
Fowl typhoid mixed bacterin	Streptococcus staphylococcus bacterin (equine)
Fowl typhoid bacterin	
Fowl typhoid and fowl cholera mixed bacterin	
	White scour bacterin (bovine)

Bacterial Vaccines (Bacterins) consist of killed bacteria suspended in physiological salt solution. Bacterial Vaccines and Bacterins used in human medicine are synonymous. A distinction is made between these terms in veterinary practice.

The specific bacteria are grown on suitable culture media the necessary length of time, usually 24 hours, after which they are washed off and suspended in physiological salt solution. The bacteria are then killed, either by heat or by chemical agents, and the suspension is diluted with physiological salt solution to contain the desired number of dead bacteria per cubic centimeter. A preservative is also added, usually 0.2 to 0.4 per cent of trikresol, phenol, or cresol solution, to prevent contamination.

Contrary to the action of true vaccines (see page 371), bacterial vaccines do not produce the disease even in a mild form. They contain the antigenic and toxic products of the bacterial cell, and produce reactions in the system in a manner similar to those following a natural infection.

The intensity of the reaction may be controlled by the size of the dose, *i. e.*, the number of bacteria injected. Successive doses stimulate in the blood of the individual a greater resistance to the invasion of the homologous species. In technical language, their use increases the opsonins in the blood. The opsonins are the elements in the blood or

body-fluids which are capable of so modifying the invading bacteria that they become ready prey to the leucocytes (white blood cells). The presence of opsonins is an important factor in natural immunity, and they may be increased artificially by the use of bacterial vaccines.

Bacterial vaccines are used both for prophylactic and for curative purposes. They are similar in their action upon the system to the true vaccines, but since no virus is introduced, the action is under better control.

Active immunity follows their use, which is similar to natural immunity in that it is generated in the body of the patient.



FIG. 82.—Diluting suspension for bacterial vaccines.

There is a large and gradually increasing list of bacterins on the market, which comprises the largest single class of biological products. The list is being augmented by new combinations of the commoner species as well as by those prepared from newly classified species.

Bacterial Vaccines are furnished either in liquid or dry form and usually are offered in different strengths. The number of dead bacteria per cubic centimeter varies greatly with the different species and with the dose desired, commonly from 20 to 2000 million or more.

Bacterial Vaccines (Bacterins) are administered in two or more successive doses, by hypodermic injection, and at intervals of 3 to 7 days. When used for prophylactic purposes, these products usually contain only one species of bacteria, but when employed for curative purposes, combinations of different species with the initial species are often preferred. These are known as mixed or combined vaccines.

It is recognized that the theory of multiple or mixed infection plays an important part in the continuation of symptoms following a specific infection. The causative organism may be present for a few days only, being supplanted by one or more secondary infectious organisms which may entirely overgrow the original causative organism. This condition has led to the introduction of mixtures intended to combat both the causative organism and also those which follow.

Thus for prophylactic purposes, or in the very early stages of a disease, vaccines prepared from a single variety of bacteria are generally sufficient, while the "mixed" or "combined" vaccines occupy a specific field as curative agents when the initial infection is liable to have been modified or obscured by secondary invasions of other varieties or species.

Bacterial vaccines are generally named from the disease or the organism against which they are directed. For instance Acne Vaccine is prepared from the specific organism of acne—*Bacillus acne vulgaris*, while Acne Vaccine Mixed (or combined) is prepared from the several species of bacteria found in the lesions of acne, such as the species of organisms believed to be the cause of acne and the varieties of staphylococci.

The above applies to the generally accepted description of the bacterial vaccines and the usual methods employed in their manufacture. The application of bacterial vaccine therapy to a wider field, in both human and veterinary medicine, thus including a larger number of species with their cultural peculiarities, has made certain modifications of the standard methods necessary.

These variations in methods may apply to those species which grow sparsely and with difficulty on solid media. Such species are therefore grown in a liquid medium and the organisms then removed en masse by centrifugalization, suspended in physiological salt solution, counted, and from then on carried through the standard process. With certain species used in veterinary practice it has been found advantageous to allow the organisms to remain in the liquid medium in which they are grown. Those products, labelled "vaccine" for veterinary use (see page 358) contain the living attenuated organisms in a suitable diluent, without any preservative.

No standards of activity are applied to Bacterial Vaccines, except typhoid and typhoid-paratyphoid vaccines. The test for activity as applied to these two consists of the actual vaccination of rabbits with three doses from representative samples from each lot of manufactured product. The injection of three doses from each lot of vaccine must produce an agglutinin titre in the rabbit serum in dilution of 1-800 to the typhoid bacillus and 1-200 to the paratyphoid bacilli "A" and "B" combined, to permit its release to the market under Government license.

The dosage of bacterial vaccines is quite generally based on their bacterial content per cc. This bacterial content varies within wide limits in the products of the several manufacturers, and serves as a guide in the administration of the product. It cannot be taken as a standard of activity because of the great variation in the antigenic qualities existing in the parent strains employed in the manufacture of vaccines by the different laboratories.

Bacterial vaccines are offered to the trade in a great variety of packages, both as to style, size, and convenience in withdrawing contents. It may be stated that the syringe container, on account of its cost, has grown less in favor, and that the single dose containers have been largely superseded by multiple dose vials, equipped with a thin rubber diaphragm cap which provides a convenient means for withdrawing any desired amount of the vaccine directly into a syringe, by plunging the needle through the rubber cap while holding the container in an inverted position.

DIAGNOSTIC AGENTS

Coincident with the increasing assistance offered by the clinical laboratory as an aid to the physician in arriving at correct diagnoses, a steadily increasing demand has occurred for products to be used in laboratory and bedside diagnosis.

The term "diagnostic agents" is quite generally applied to these biological products, regardless of their particular nature.

Among these products are, Antigens and Amboceptors, for making the complement fixation (Wassermann) test; suspensions of killed bacteria to be used in determining the agglutination titre of serums from patients suspected of being infected; antibacterial serums with which to check, by agglutination, the particular species, or the type of a given species of organism causing infection; Antihuman Precipitin Serum, with which to identify human blood in medico-legal practice; Human Blood Typing Serum to determine the type of blood of the recipient and donor before blood transfusion; Protein Extracts, Diagnostic; Tuberculins; Diphtheria Toxin for the Schick test, and Scarlet Fever Toxin for the Dick test.

It may be ventured at this point that the above list will be augmented by new products of biological origin which will come into use as a result of extensive researches in medical bacteriology and biochemistry.

Antigens.—Those antigens most extensively employed are for the laboratory complement fixation test in the diagnosis of syphilis, and are extracts of tissue. Originally hearts and livers from syphilitics were employed, but later it has been found possible to prepare equally as sensitive antigens from normal tissue, principally beef heart. These tissue-extract antigens are used both in the complement fixation test, as represented by Kolmer Antigen, Cholesterinized Antigen, Plain Alcoholic Antigen and Acetone Insoluble Antigen; and in the precipitation test which requires Kahn Standard Antigen and Kahn special antigen.

Antigens of bacterial origin are also employed in the complement fixation test for the diagnosis of diseases, and represent extracts of bacterial bodies. In this class of antigens, Tubercle Antigen is offered for the serological diagnosis of tuberculosis, and Gonococcus Antigen for a similar test for evidence of gonococcus infection. Antigens are usually put up in 5 cc. bulbs.

Amboceptors.—This group of diagnostic agents consists of anti-serums, prepared by immunizing rabbits or other animals with serum-free corpuscles from the same species of animals from which washed

corpuscles are to be used in the complement fixation test. Those amboceptors in most general use are Antisheep Amboceptor, coupled with sheep corpuscles for use in the complement fixation test and Antihuman Amboceptor, when it is desired to use human red blood corpuscles for making the test (Noguchi modification of the Wassermann test).

Antihuman Precipitin Serum.—This serum is prepared by immunizing rabbits with repeated injections of increasing amounts of human serum. A specific quality is produced in the rabbit serum which gives a precipitate when mixed with human serum. This diagnostic serum is employed in medico-legal cases when it is desired to establish the identity of blood stains, suspected of being of human origin, and is usually supplied in 1 cc. bulbs.

Human Blood Typing Serums.—It is known that the blood of human beings falls into four groups, these being differentiated by corpuscle agglutination. When certain groups are mixed, as in blood transfusion, objectionable results may follow on account of the agglutination of corpuscles. Through the use of diagnostic serums representing two of the groups, it is possible, by cross agglutination tests, to determine to which group any individual's serum belongs. Typing serums representing these two groups are now available, with which the blood of the donor and the recipient may be typed before transfusion, and a donor of the proper type selected whose blood does not cause objectionable reaction in the recipient. Human blood typing serums, representing types 2 and 3 according to Jansky's classification, are obtainable in capillary tubes in quantities sufficient for a single classification, and in 1 cc. bulbs suitable for hospital use.

Tuberculins.—Tuberculins for use in diagnosis are represented principally by Tuberculin Old. In the **Moro Test**, the Tuberculin Old is applied in the form of an ointment to the skin; the **Calmette test** is made with Tuberculin Old in a purified form, in either solution or small tablets, dropped into the conjunctiva of one eye; **Von Pirquet Test** requires Tuberculin Old in liquid form, for application to a superficial scarification of the skin; a subcutaneous Tuberculin Test involves the subcutaneous injection of diluted Tuberculin Old; and the **Mendel and Mantoux test** consists of the injection of diluted Tuberculin Old in the superficial layers of the skin.

Protein Extracts, Diagnostic.—These extracts represent the protein, extracted by various methods, from bacterial cultures, foods, epidermal substances, pollens, condiments and other substances to which certain individuals develop protein sensitization.

This group of agents, which represents a large list of individual products, are supplied in solution, in powder form, and as a paste, in suitable containers of enough material for several tests. The tests are made by rubbing a small amount of the extract into superficial scarifications of the skin. Their diagnostic significance lies in a cutaneous reaction to the protein or proteins to which the individual is sensitive. To facilitate the elimination of those extracts to which the individual is not sensitive, group proteins representing a mixture of several extracts of like kind, are also supplied.

Diphtheria Toxin for the Schick Test.—This toxin is prepared by identically the same methods as in the production of toxin for

immunizing horses for the production of diphtheria antitoxin. It is then aged in a cold chamber, accurately standardized to establish its definite M.L.D. to 250 Gm. guinea-pigs, and made available in packages which provide the original toxin sufficient for 10 to 50 tests in one vial, with a separate vial of diluent with which the dilution of the toxin can be made just prior to use. This method of distributing Diphtheria Toxin for the Schick Test is necessary because of the rapid deterioration which takes place in the diluted product and the small amount— $1/50$ of an M.L.D. required for the test.

The susceptibility of individuals, principally children, is determined by injecting the toxin intracutaneously. A reaction indicates a lack of sufficient natural antitoxin in the blood to protect against infection, and that individual is pronounced susceptible to diphtheria.

Scarlet Fever Streptococcus Toxin for the Dick Test.—The filtrate from bouillon cultures of the scarlet fever streptococcus contains a toxin of decided specific activity for injection intracutaneously into individuals susceptible to scarlet fever. This toxin is standardized by intracutaneous injection of high dilutions of the filtrate, into the arms of susceptible individuals, to determine the dilution at which 0.1 cc. will give a reddened area at the site of inoculation, 10 to 20 millimeters in diameter, in 48 hours. This amount of toxin is called one skin test-dose (1 S.T.D.).

For diagnosis, one S.T.D. contained in 0.1 cc. volume is injected intracutaneously into the individual's arm; the presence of a reaction indicates that the individual is susceptible to scarlet fever, while the absence of a reaction is recognized as a sign of natural immunity toward the disease.

Scarlet Fever Streptococcus Toxin for the Dick test is available in vials containing sufficient toxin for 10–50 doses, with separate vial of diluent for preparing the proper dilution. It is to be noted that the Dick test is made by the same technic as in the case of diphtheria toxin for the Schick test, and a reaction in susceptible individuals is of the same general character.

Suspensions of Bacteria for Agglutination Tests.—Killed, preserved suspensions of bacteria of definite bacterial count. Such suspensions, particularly of the typhoid bacillus, paratyphoid bacillus "A," and paratyphoid bacillus "B," are of value in testing the blood of patients for the presence of agglutinin which develops in the blood of an infected individual. By mixing the patient's serum in proper dilutions with these three suspensions, it is possible with a considerable degree of accuracy to differentiate the species or type responsible for the infection.

Diagnostic suspensions may be obtained in bottles which provide for several tests in the laboratory; also in more concentrated form for quicker results at the bedside (Bass Watkins typhoid agglutination test).

Diagnostic Antibacterial Serums.—

Antimeningococcic serum representing 4 groups.

Antityphoid serum.

Antiparatyphoid "A" serum.

Antiparatyphoid "B" serum.

Antipneumococcic serums, 3 types—I, II, and III.

Antidysenteric serums, 3 types,—Shiga, Hiss Y and Flexner.

In addition to this list a number of other like serums are prepared for culture differentiation.

Such serums are usually obtained in limited quantities from rabbits, immunized by the injection of repeated and gradually increased doses of the respective cultures, until the blood serum of the rabbit contains specific agglutinin in definitely measurable quantities.

The use of diagnostic antibacterial serums is confined almost entirely to the culture laboratory for the identification and differentiation between strains of the same species and other species with similar cultural characteristics. Antipneumococcic serums types I, II and III are also frequently used to determine, early in the course of the disease, the type causing a pneumonia.

These serums are available in 5 and 10 cc. vials, and require laboratory facilities and equipment for their proper use. They are comparatively unstable and are rarely stocked by the druggist.

ECTO-ANTIGENS

Since the first clinical use of bacterial vaccines, it has been observed that more or less severe local, as well as general reactions, follow their injection. These reactions are attributed to the toxic portion of the vaccine, and their connection with therapeutic response is open to question. An early opinion predicted the ultimate separation or dissociation of the toxic fraction of bacterial vaccines from their specific antigenic content, which, if accomplished, would remove their most objectionable feature and at the same time permit of a more intensive scheme of dosage without the objectionable local and general reactions. This principle is the basis for the development of ecto-antigens, which are licensed as Bacterial Antigens made from gonococcus, pertussis bacillus, pneumococcus, staphylococcus and streptococcus respectively. The commercial products are marketed under the name Immunogen, representing single species and combinations of species as follows:

Bacterial Antigen made from	gonococcus—Gonococcus Immunogen.
“ “ “ “	gonococcus, staphylococcus aureus and staphylococcus albus—Gonococcus Immunogen (Combined).
“ “ “ “	pertussis bacillus—Pertussis Immunogen.
“ “ “ “	pertussis bacillus, staphylococcus aureus and staphylococcus albus—Pertussis Immunogen (Combined).
“ “ “ “	pneumococcus (3 types)—Pneumococcus Immunogen.
“ “ “ “	pneumococcus (3 types); streptococcus (hemolytic and non-hemolytic)—Pneumococcus Immunogen (Combined).
“ “ “ “	streptococcus (hemolytic and non-hemolytic)—Streptococcus Immunogen.
“ “ “ “	streptococcus (hemolytic and non-hemolytic); staphylococcus aureus and staphylococcus albus—Streptococcus Immunogen (Combined).

Pure cultures of the strains to be used in the production of immunogens are grown on solid nutrient media, washed off with a minimum amount of physiological salt solution, and the washings immediately removed and diluted to a standard, based on bacterial count per cc. of the suspension before washing.

A preservative is then added to the water-clear bacteria-free ecto-antigen solution. Each lot of product is made to conform to a uniform standard based on bacterial count of the organisms contained in the original suspension.

The immunogens are supplied in 10 cc. rubber diaphragm-capped bulbs to provide a sliding scale of dosage from 0.5 cc. to 5 cc.

HEMOSTATIC AGENTS

Coagulose

Hemostatic Serum (LaPenta) (Hemoplastin)

Normal Serum

Excessive bleeding following minor cuts or abrasions, tooth extractions, minor and major operations, and in diseased tissue, is usually due to faulty coagulation of the blood on account of lack of balance of the constituents which promote normal coagulation.

Specific agents intended for the control of hemorrhage come under two distinct classes—preparations intended to be used by local application, and those products of biological origin which are distributed under U. S. Government license with recommendation to be injected to correct the cause of such lack of coagulability.

Under hemostatic agents, only the latter group will be considered.

Precipitated Horse Serum, Coagulose.—This serum is prepared from the clear fresh serum collected from horses whose blood possesses an average normal coagulation time. In the precipitation process the serum is reduced to a water soluble anhydrous powder, which retains its power to check hemorrhage over long periods of time.

The sterile tested product is supplied in bulbs of sufficient capacity to permit of the addition of 10 cc. of sterile warm water to dissolve the powder immediately before use. Each vial contains powder equivalent to 10 cc. of fresh normal horse serum.

Hemostatic Serum (LaPenta) Hemoplastin.—A serum product derived from the blood serum and tissue from both horses and cattle which contains those essential constituents necessary to reduce the coagulation time of blood.

Hemostatic serum is a water-clear, sterile solution of low protein content. Each lot of product is standardized by determining the degree to which a two cc. dose injected intravenously will reduce the coagulating time of the blood of a normal dog. No lot of product is released for use unless it will reduce the coagulating time of the blood of a normal dog to one-third of the time the blood required to coagulate prior to the injection of the sample under test. It is supplied in 2 cc. and 5 cc. bulbs and is recommended for subcutaneous or intravenous injection.

Normal Serum.—Normal serum from rabbits, horses and other animals has been used for many years to check or prevent hemorrhage. Its use has been limited, because best results follow the injection of strictly fresh serum, which entails the necessity of obtaining supplies direct from the producing laboratories with a coincident objectionable loss of time. Normal serums are supplied in syringes and bulbs of various capacity as specified by the physician.

MODIFIED BACTERIAL PRODUCTS

Sero Bacterins
Sensitized Vaccines
Phylacogens

It will have been noted that in the treatment of disease by means of biological products the main endeavor is to raise the resistance of the patient by artificially increasing the immune bodies in the circulating fluids. This is done in two ways: by introducing the immune bodies, to give passive immunity, through the injection of a fluid containing them, as in the treatment of diphtheria with diphtheritic antitoxin, or by actively increasing them by stimulating the patient's own resistant powers to produce more of their own immune bodies by the use of vaccines, toxins, etc. These treatments are known as serum therapy and vaccine therapy, respectively.

The first produces a degree of immunity at once, which is comparatively transitory in character. The second produces immunity after a certain time, more lasting in its effects.

Attempts have been made to combine the advantages of the two, and at the same time to eliminate their disadvantages. In 1892, mixtures of certain organisms in their antisera were tried, but with little success. In the mixture there appears to be an interference in action between the bacteria and the antiserum, and a combination of the two is therefore of little or no advantage, and may even be disadvantageous.

Sensitized Vaccines.—In 1902, Besredka, working in the Pasteur Institute, first produced a form of bacterial vaccine which he called "sensitized vaccine." This is made by growing a pure culture of the bacteria on agar, and then washing it off with physiological salt solution, effecting a suspension of living bacteria. To this suspension is added a certain amount of antiserum, produced in the same manner as an antibacterial serum is produced by action of the germ on the living body of an animal. The living germs will absorb a certain amount of the antibodies and become sensitized. After 12 to 24 hours the germs are sedimented and washed with fresh salt solution to remove all the adhering serum. The germs are then killed and suspensions are prepared in the same manner as bacterial vaccines.

The action of these sensitized bacterial vaccines is little understood. It is thought that phagocytosis is promoted and that the leucocytes are activated, and thereby immunity is brought about more quickly. These sensitized vaccines are now being sold under the name of Sero-bacterins, of which there are several varieties. They are employed in the same manner as the bacterial vaccines, but are usually given in larger doses.

These products are made from a large number of species of bacteria and supplied in packages similar to bacterial vaccines. Their bacterial content is also made the basis of dosage.

Phylacogens, or Modified Bacterial Derivatives, Schafer.—

Erysipelas Phylacogen.
Gonorrhea Phylacogen.
Mixed Infection Phylacogen.
Pneumonia Phylacogen.
Rheumatism Phylacogen.

Mixed Infection Phylacogen, Veterinary.**Pneumonia Phylacogen, Veterinary.**

These originated with Dr. A. F. Schafer of Bakersfield, Cal., who believed that most infectious diseases are due to a mixed infection, one species of germ predominating, while the others or secondary species contribute to the severity and prolongation of the disease, and that the predominating germs determine only the type of the disease.

These products are neither bacterial vaccines nor serums, as generally understood. They are sterile aqueous solutions of so-called bacterial derivatives generated by bacteria grown in artificial media. The bacteria are killed and filtered out with germ-proof filters. They thus resemble the extractive tuberculins in their character and mode of preparation.

Phylacogens are marketed in 10 cc. vials for use on humans and in 30 cc. bottles for veterinary administration.

Pollen Extracts for Desensitizing.—The nitrogenous portion of pollen grains is extracted with water, weak alkaline solution, or glycerin, and serves in proper dilutions for the desensitizing treatment of individuals previously demonstrated to be sensitized to a certain pollen or pollens through the use of diagnostic Pollen Extracts.

The extraction is accomplished under aseptic conditions in the presence of a suitable preservative, after which the extract is filtered through germ proof filters.

Each lot of extract is standardized on the basis of weight of original pollen represented in each cc. of extract, or by weight of nitrogen in the final product.

The completed extract is supplied in a sterile powder, or in glycerin solution, accompanied by vials of physiological salt solution to provide a convenient means of arriving at the desired dilutions with which to begin the injections.

Protein Extracts for Desensitizing.—The nitrogenous extracts of bacterial cultures, foods, epidermal substances, condiments and substances other than pollens, are prepared similar to pollen extracts for use in the desensitization of individuals found to be sensitive to any given protein.

The total protein content of each extract is determined to give a basis for proper dilutions for treatment.

The sterile extracts are supplied in small bulbs, with vials of diluent to provide for freshly made dilutions immediately before use.

TOXINS

Diphtheria toxin for the Schick Test (see diagnostic agents, page 362).

Diphtheria toxin-antitoxin mixture.

Mallein

Scarlet Fever Streptococcus toxin for the Dick test (see diagnostic agents).

Scarlet Fever Streptococcus toxin for immunization.

Under this heading only those products which derive their activity from toxin, alone or in combination, will be considered. The tuberculins will be covered under a separate heading.

Diphtheria Toxin-antitoxin Mixture.—Long before the practical value of a mixture of diphtheria toxin and antitoxin, in the prophylactic immunization of susceptible individuals against diphtheria, was recognized, extensive work with the immunization of horses with neutralized mixtures had demonstrated that the neutralization of a diphtheria toxin with its antitoxin does not destroy or remove that quality in the toxin which stimulates antibody formation. This quality still exists in the neutralized toxin-antitoxin mixture and makes possible adequate lasting immunization against diphtheria infection.

Diphtheria toxin-antitoxin mixture is made by combining well aged sterile diphtheria toxin with sterile tested antitoxin of high potency. The aged toxin is first diluted with physiological salt solution to give a resultant toxin each cc. containing $1/10$ L+ dose of toxin. Only sufficient antitoxin of high potency is then added to the diluted toxin to bring about neutralization to a degree that 1 cc. of the mixture will not kill a 300 gram guinea-pig within 35 days, while 5 cc. of the mixture will kill the pig in 8 to 12 days. The mixture is accurately adjusted to this definite point of neutralization by adding more antitoxin if necessary.

The final sterile clear product is usually marketed in syringes, bulbs and vials of 1 cc. each. Three 1 cc. doses constitute a complete immunizing treatment. The product is also furnished in vials of 10 cc. to 30 cc. for use in groups where a large number of doses are required at one time.

Mallein—Veterinary

Glycerin bouillon cultures of bacillus mallei of glanders are concentrated over a steam bath to one-tenth of their original volume and filtered through germ-removing filters. The resulting clear dark amber colored fluid in its final concentration contains 50 per cent glycerin which serves as a preservative.

This product, when injected in small doses into animals suffering from glanders, produces a toxic reaction specific to glandered animals and constitutes the Mallein test.

Mallein is supplied in both liquid and dry forms for detecting glanders in horses and mules.

In the liquid state it is applied by subcutaneous injection and by intrapalpebral injection (in the layers of the skin). The subcutaneous injection produces a reaction in infected animals which is detected by a rise in temperature of 2 degrees or more above normal, while a positive reaction to the intrapalpebral test is evidenced by swelling and soreness at the site of injection.

Liquid mallein is supplied in vials of 1 cc. and 2 cc.

Mallein in a precipitated dry form is incorporated with milk sugar and made into discs for use in the eye test for glanders. One disc is placed in the conjunctival sack of one eye of the suspected animal and a positive reaction detected by a pronounced reddening and inflamed condition of the test eye.

This product is furnished in vials of 5 or more discs.

Scarlet Fever Streptococcus Toxin.—This product is used to effect a prophylactic active immunization of individuals found susceptible to scarlet fever by the Dick test.

The toxin is prepared by growing strains of the scarlet fever streptococcus in a suitable medium after which the bacterial bodies are removed by filtration. Its activity is expressed in terms of skin test doses (S.T.D.) per cc., upon which value the series of doses for immunization is calculated.

The final product is supplied in 1 cc. doses of toxin in serial strengths, varying from 500 skin test doses for the initial dose to 30,000 or more skin test doses per cc.

TUBERCULINS

Tuberculin B. E. (Bacillus Emulsion).

Tuberculin B. F. (Bouillon Filtrate).

Tuberculin Old, Koch.

Tuberculin T. R. (Tuberculin Residue)

Tuberculin, Veterinary.

Numerous preparations, derived from pure cultures of the tubercle bacillus, have been developed and submitted to use, only to be discarded as of questionable value in the treatment of tuberculosis.

After years of experimental effort, a limited number of such preparations have been accepted as being of some value in certain patients whose resistance will permit of the specific stimulation afforded in tuberculin therapy. These products may be referred to as **extractive** and **residual**, and represent fractions of cultures of the tubercle bacillus from both human and bovine sources which have been grown at body temperature for a number of weeks in glycerin bouillon.

Extractive Tuberculins are derived from the clear filtrate from cultures while the residual tuberculins are made from the culture mass.

Tuberculin B. E. (Bacillus Emulsion).—The living organisms are removed from the bouillon culture and washed to rid the mass of traces of the bouillon in which growth took place. The organisms are dried and then ground in a suitable mill to effect destruction of the individual cells. The ground material is either suspended in sterile 50 per cent glycerin solution or mixed with suitable excipient for use in a dry form.

The strength of Tuberculin B. E. is reckoned from the total solids and is expressed in mgs. of disintegrated bacilli per cc. of emulsion or per gram of the dry product.

Tuberculin B. E. is supplied in 1 cc. bulbs containing 1 mg. to 5 mgs. total solids per cc., from which the desired dilutions, for dosage, may be prepared. This product is also made available in the dry form in tablets, which provide convenient means for arriving at an accurate scheme of dosage based on a definite percentage increase over preceding dose. The tablets are of five strengths, ranging from 1 mg. to 0.0001 mg. of Tuberculin B. E. per tablet. They are supplied in vials of 10 tablets.

Tuberculin B. F. (Bouillon Filtrate).—A clear, amber colored solution, representing the bouillon in which the tubercle bacillus has grown, is obtained by filtering the culture free from organisms. This filtrate contains the soluble products elaborated in the medium. A suitable preservative is added to prevent contamination.

Tuberculin B. F. is supplied in 1 cc. bulbs from which any desired dilution may be made before injection.

Tuberculin Old, Koch (see *Diagnostic Agents*, Page 362).—This, the most widely used Tuberculin for both therapeutic and diagnostic purposes, is prepared by concentrating whole glycerin bouillon cultures of the tubercle bacillus to one-tenth of the original volume over a steam bath. During concentration the organisms are killed by the heat and the content of glycerin increased to 50 per cent.

After the concentration process is complete the dead organisms are removed by filtration, and the dark amber solution is tested for sterility and made ready for distribution as Tuberculin Old, or to the various uses as a diagnostic agent.

Tuberculin Old, for therapeutic use, is usually supplied in bulbs of 1 cc. to 10 cc. capacity. Before use it is necessary to make serial dilutions to provide the desired dosage for each individual under treatment.

Tuberculin T. R. (Tuberculin Residue).—A residual tuberculin, prepared very similar to Tuberculin B. E. except that the water soluble fraction of the disintegrated bacilli is removed by repeatedly grinding, extracting and sedimenting the germ mass. After each sedimentation the clear supernatant liquid is removed and discarded, thus eliminating the water soluble portions of the ruptured organisms. The degree of disintegration is determined by microscopical examination of stained specimens taken from the sedimented residue.

Tuberculin T. R. then represents the finely divided water insoluble residue obtained from the last sedimentation process. The final preparation is diluted to contain from 1 mg. to 10 mgs. total solids per cc. in physiological salt solution; 20 per cent of glycerin is added as a preservative. It is sold in 1 cc. bulbs, also in a dry form in tablets of varying strengths similar to tuberculin B. E. Dilute Tuberculin T. R. is also available to the trade in bulbs of 1 cc., each bulb containing 0.001 mg. of tuberculin residue.

Tuberculin Veterinary.—In veterinary practice the use of tuberculin is confined exclusively to diagnosis. Several methods are advocated for conducting diagnostic tuberculin tests on domestic animals, which require tuberculin in such concentration that will serve each particular method of test. These various tests include the subcutaneous and intradermic injections, which require tuberculin in the liquid form, and the eye test for which discs containing tuberculin in a dry form are provided. Regardless of the test method, the tuberculin employed is essentially Tuberculin Old, Koch, in varying degrees of concentration and form in which it is made available for use.

Tuberculin (Subcutaneous).—A product concentrated to four-fifths of its original volume and supplied in multiple dose vials of 20 cc. to 100 cc. to provide doses of 2 cc. to 7 cc. depending on size of animal.

Tuberculin (Intradermic).—Similar in concentration to Tuberculin Old, Koch (one-tenth of original volume) is supplied in vials of 1 cc. to 5 cc. to provide multiple doses of 0.1 cc. to 0.2 cc. for intradermic injection.

Tuberculin (Ophthalmic).—By a method of precipitation, filtration and desiccation the active principle of Tuberculin Old is reduced to a powder, which is incorporated with milk sugar to make tablets or discs of suitable size for inserting into the conjunctival sack of the

animal's eye. Each disc or tablet contains enough of the active principle of old tuberculin to provide a sensitizing dose, while two tablets or discs are used to make the actual test. The final product is usually supplied in vials of 10 discs each.

VACCINES

The vaccines, sometimes called "true" vaccines, are the products resulting from a modifying or attenuating process and are intended solely for prophylactic or preventive use. They are to be administered sufficiently in advance of the onset of the disease to permit of the



FIG. 83.—Taking vaccine from the calf.

development of active immunity. They are not employed as curative agents.

Smallpox Vaccine

In the manufacture of smallpox vaccine healthy calves or heifers are selected, quarantined for several days, tuberculin tested and thoroughly examined for evidence of disease. At the end of the quarantine period each animal is clipped and transferred to the preparation room, where its entire body is scrubbed and cleansed with warm water and a germicidal soap.

From the preparation room the animal is taken to the operating room and placed on a special operating table, so constructed as to per-

mit of shaving and sterilizing the abdominal surface. The "seed" virus is rubbed into shallow linear incisions with a sterile instrument, after which the vaccinated animal is removed to the propagating room. Here it remains at a constant room temperature for a period of 7-8 days to allow a maximum development of vaccinia vesicles. An attendant is constantly present both day and night to avoid contamination of the vaccinated area.

At the end of the propagation period, the animal is returned to the operating table and killed immediately before removing the vaccine pulp (vesicles). The removal of the pulp is accomplished by means of a sterile curetting spoon after the vesicles have been uniformly softened



FIG. 84.—Grinding smallpox vaccine.

with warm sterile water. The pulp is collected in sterile glycerin solution and transferred immediately to a storage chamber maintained at a temperature below freezing. It is then reduced to a definite degree of fineness in 50 per cent glycerin solution by grinding or triturating, and then allowed to remain at below freezing temperature until the foreign bacterial content has been reduced by the germicidal action of the glycerin to a standard of purity established by regulations imposed by the Hygienic Laboratory.

Directly after removing the pulp, a thorough postmortem examination is made of the animal carcass, to verify the tuberculin test and to give assurance that the animal was free from evidence of disease. Only such lots of vaccine as come from absolutely normal animals is permitted to be distributed.

The propagating and operating rooms of a smallpox vaccine plant are constructed, equipped, maintained and supervised in keeping with approved hospital practice to eliminate contamination of the pulp with pathogenic micro-organisms.

Smallpox Vaccine is Extremely Sensitive to Heat.—It deteriorates very rapidly unless stored at refrigerator temperature. It is labelled with a short dating incumbent upon the temperature at which the finished package is stored. Long shipments are to be avoided in the



FIG. 85.—Tuberculins,—extractive and residual.

summer months unless packed in ice or transported in refrigerator chambers or cars.

Exactng tests are imposed on the manufacturers of smallpox vaccine through Government Regulations to assure a product free from pathogenic bacteria.

Smallpox Vaccine, Dry

Increasing demands for vaccine in territories remote from manufacturing laboratories are being met with a desiccated product. The methods of preparation do not differ materially from the glycerinated vaccine, except that the "aging" is accomplished without the use of glycerin. By a carefully controlled drying process, the active principle of the vaccine is preserved sufficiently to promote better keeping

qualities, to allow a longer dating and to provide for transportation where refrigerator facilities are not available.

Anthrax Vaccine, Veterinary

Living cultures of the anthrax bacillus, if grown at a temperature higher than that of the living body, become attenuated sufficiently to permit of their being injected without producing the disease. This principle announced by Pasteur in 1881 is the basis for the production of anthrax vaccine. The organisms are obtained from a typical case of anthrax and grown in an artificial culture medium at 42° C. in repeated generations until the organism loses its virulence to test animals. This vaccine is usually prepared in two strengths and is called a double vaccine; dose No. 1, the more attenuated, to be used first, followed after a few days by No. 2, the stronger dose.

Anthrax vaccine is employed only in veterinary practice as a preventive measure against anthrax. Its use is not entirely devoid of danger, because of the wide variation in the resistance of individual animals and the effect of adverse conditions and care to which domestic animals may be subjected prior to or immediately after injection of the vaccine.

The final product is a suspension of living attenuated spores in a suitable solution. It may be used alone or in conjunction with anti-anthrax serum by the simultaneous method. It is supplied in multiple dose packages to be used alone, or with antianthrax serum by the simultaneous method.

Blackleg Vaccine, Veterinary

In principle, this vaccine is similar to Anthrax Vaccine in that the spores of the organism causing blackleg permit of being attenuated by heat without losing the power of producing active immunity. Blackleg Vaccine may be prepared from the infected muscle tissue of bovines dead of the disease, or from the spores produced in artificial culture media. Attenuation is accomplished by prolonged heating (usually 6 hours) at a temperature range between 85° and 95° C. (93.5° C., U. S. Government regulations). This product is offered, as a liquid suspension, as pellets consisting of the dry heated muscle virus, as absorbent threads impregnated with the attenuated spores, and as attenuated muscle "virus" in powdered form, in multiple dose packages for prophylactic immunization against blackleg.

Man is not susceptible to blackleg, hence this product is used only in veterinary practice, principally on cattle and sheep.

Rabies Vaccine

Rabies vaccine was originated by Pasteur in 1885. The virus of rabies is of unknown character and is contained in the brain and spinal cord of animals suffering from or dead of rabies (hydrophobia). The virulence of this virus is increased to a fixed standard by the original method of Pasteur, which consists of repeated passage through rabbits until it will kill a rabbit in about 6 days. After reaching this degree of virulence, it becomes comparatively stable and is called "fixed"

virus, providing a fortunate basis for the standard of attenuation. The brain, spinal cord or both, removed under aseptic precautions from an animal killed with "fixed" virus, are used in the preparation of rabies vaccine.

Since Pasteur gave this life saving discovery to the world, rabies has lost its former dread, and fatalities following exposure to rabies have been reduced to a fraction of one per cent.

The vaccine is made available in several forms, some of which are decidedly unlike the original Pasteur vaccine.

Pasteur's method, as now employed, gives a vaccine prepared from the spinal cord of a rabbit killed with "fixed" virus. The cord is removed with aseptic precaution and dried over sticks of caustic potash in sterile jars at a temperature of about 22° C. (70° F.) for periods varying from 2 to 8 days. Doses, ranging from 1 cm. to one-third cm. of the dried cord, are given at 24 hour intervals; the cords dried for the longest time are used for the first series of doses, followed by doses taken from the lesser attenuated cords, until treatments covering 21 days have been given. This constitutes the intensive treatment used in severe exposures produced by deep lacerations of the face or arms, while as few as 14 daily treatments are given when the patient is exposed to mild injuries to the lower extremities or through the clothing.

Pasteur Rabies Vaccine is administered in Pasteur Institutes in various parts of the world, in municipal health laboratories, and is also made available to remote locations by mail through daily shipments of single doses of the properly attenuated cord in suitably preserved suspension in correct sequence.

Hogyes Dilution Method involves a somewhat different principle of safely vaccinating against rabies. The fresh virulent cord, in physiological salt solution suspension, is diluted sufficiently so that a dose of the dilute suspension will not produce rabies in test animals. This constitutes the first dose, which is followed by succeeding doses containing more and more of the rabid brain virus. In the preparation of this vaccine no attenuation of the virus takes place; the dilution of the virus merely reduces the amount of virus injected to a margin of safety.

Harris' Desiccated Rabies Virus represents a modification of the Pasteur vaccine in that the brain and cord are ground in the presence of carbon dioxide snow, and the frozen tissue then transferred to a vacuum drying apparatus where it is reduced to complete dryness at a temperature of 18° C. This drying process reduces the tissue to a powder and causes the virus to lose about one-half of its original virulence.

Harris' Vaccine is standardized in units, one unit being that quantity of the powder that will infect a rabbit when injected intracerebrally. Before use a definite weight of the powdered virus for each dose is suspended in salt solution.

Marie's Virus-serum mixture is a combination of fixed virus suspension and antirabic serum and is used as the first daily injections in conjunction with Pasteur vaccine. The advantages claimed for it are that it gives rise to early immunity in cases of severe exposure.

Rabies Vaccine, Cumming.—In the preparation of this vaccine dialysis of the brain suspension renders the virus non-infectious to animals receiving relatively large doses of the dialyzed vaccine intracranially.

The suspension is standardized by weight to contain 1 per cent of brain substance. This method of preparation enables the manufacturer to produce a vaccine free from bacterial contamination and of a definite dosage of 2 cc. for each of 14 or 21 daily injections. It is supplied in 2 cc. syringe containers and shipped in packages of 7 doses at necessary intervals to avoid undue exposure at room temperature.

Rabies Vaccine, Cumming is sufficiently stable to permit of its being carried in cold storage at various convenient points, thus rendering it quickly obtainable. It possesses distinct advantages over the attenuated forms of rabies vaccine in that it is non-infectious, sterile, and all doses are alike, thus avoiding the possibility of mistakes in dosage.

Rabies Vaccine Veterinary.—The extensive research investigations of Semple have made available on a practical basis rabies vaccine for the prophylactic vaccination of unexposed dogs and other domestic animals, and the preventive inoculation against rabies in those animals exposed to the disease.

These vaccines are prepared from the brains and cords of rabbits and dogs killed with fixed virus. The different vaccines vary considerably with respect to the percentage of brain and cord substance contained in each 5 cc. dose. This variation ranges from 5 to 20 per cent.

Veterinary rabies vaccines are principally intended to be employed as a single dose prophylactic inoculation of normal animals against possible subsequent exposure to rabies. Statistics compiled in crowded localities where rabies is normally quite prevalent, indicate that the use of these vaccines, as a means of controlling rabies, particularly in the dog, gives promise as an efficient aid in preventing the spread of this dread disease.

Hemorrhagic Septicemia Vaccine Veterinary.—The effect of a single injection of killed bacterial cells conveys an initial mild degree of immunity. This principle is also applied to the use of a living vaccine as a prophylactic inoculation of domestic animals against hemorrhagic septicemia. This vaccine is employed as the second dose in conjunction with hemorrhagic septicemia bacterin but is not to be used alone.

Cultures of the virulent organism are grown in a suitable culture medium, the number of organisms per cc. of the resulting suspension estimated by bacterial count and adjusted to a definite standard. The activity of this vaccine depends upon its content of living virulent organisms, hence no preservative is added.

The vaccine is standardized by bacterial count to contain 5000 million or more organisms per cc. and is supplied in vials of 20 cc. to 100 cc. to afford elasticity in dosage, usually from 2 cc. to 4 cc. depending on size of animal to be treated. The large containers also provide sufficient product to treat several animals. It is conceded that this vaccine should be used for prophylactic purposes only.

Contagious Abortion Vaccine Veterinary.—Contagious abortion in dairy herds has come to be recognized as a problem of far reaching proportions, both from the standpoint of economic loss and public health. Owing to the peculiar nature of the causative organism—*Bacillus abortus* (Bang), efforts to combat the disease with products made from the organism, have proved disappointing. While Bacterins and Vaccines have been used to some extent and are still available to the

veterinarian, results following their administration leave much to be desired.

Need for more active agents to stimulate a higher degree of immunity, has resulted in the employment of living suspensions of the organism, a vaccine prepared from cultures of varying virulence. Such vaccines may be obtained in multiple dose vials of 20 cc. and 200 cc.

Hog Cholera Virus (See Page 354 Anti Hog Cholera Serum) Veterinary.—The exact cause of hog cholera has not as yet been determined. It is known, however, that a filtrable virus is uniformly found in the blood of swine suffering from this disease. This virus is extremely infectious and may be maintained indefinitely by the transfer, at regular intervals, of infected blood to normal animals.

Normal pigs injected with a non-lethal dose of hog cholera virus are rendered actively immune to subsequent attacks of cholera. This principle forms the basis for the commercial virus, which is recommended only as a prophylactic immunizing agent in combination with anti hog cholera serum, but injected separately by the simultaneous method. Hog Cholera Virus used in conjunction with the serum produces an early passive immunity, followed by more lasting effect.

The virus is supplied in 20 cc. to 40 cc. vials which provide multiple doses of 1 cc. to 2 cc.

Chicken Pox Vaccine Veterinary.—This vaccine is used for treatment and prevention of chicken pox. It is made by emulsifying 1 Gm. of powdered desiccated virus (scabs from lesions in birds suffering from chicken pox) in 100 cc. of physiological salt solution. The dose is 1 cc. subcutaneously to each bird at intervals of 3 to 5 days. It is marketed in packages of 20 cc., 50 cc. and 100 cc. No method of standardization.

Chicken Pox Virus Veterinary.—For use as a preventive of chicken pox. It is represented by desiccated scabs from lesions of chicken pox. Birds are inoculated by rubbing the virus into scarifications on tip of comb. The lesions are cut off at the end of the tenth day and distributed. No method of standardization.

MISCELLANEOUS PRODUCTS

Lactic Acid Products.—It is scarcely necessary to state that lactic acid bacteria have been used to modify certain foods, particularly milk, for centuries. Late in the nineteenth century these forms of microbial life were recognized by many as having beneficial effect on the intestinal flora.

Three species of lactic acid bacteria have been and are still being used extensively, even though wide differences in opinion exist as to their relative merits.

Bacterium Acidi Lactici, Streptococcus Lacticus.—These names apply to the common lactic acid bacillus which is easily isolated from practically all dairy products, grows luxuriantly in sterile milk, whey, and nutrient media, produces a moderate degree of acidity, and is capable of imparting a pleasing flavor and consistency to whole milk.

Characteristically active strains of this species have been selected with due regard to flavor and curd consistency for the production of

buttermilk "starters" in tablet, powder and liquid forms. These "starters" are prepared by growing the selected cultures in bouillon, agar, whey medium, or in sterile milk, after which the heavily implanted mass is distributed as liquid culture or is reduced to complete dryness under conditions that will not prove injurious to the living organisms. The powdered product is usually obtainable in 1 oz. containers; the tablets, in vials containing various numbers of tablets.

Practically all milk supplies contain objectionable contaminating organisms. These "starters" added to the whole milk provide a rich implantation with lactic acid bacteria which in turn produce an acidity ample to hold the growth of the contaminating organism in check, and a smooth creamy "buttermilk" results.

The direct value of the common lactic acid bacteria buttermilk, in correcting faulty intestinal flora, is open to question, although many habitual users of buttermilk maintain that a cumulative effect is produced, which in turn reduces the objectionable putrefactive changes in the colon.

Buttermilk made from these "starters" contains essentially the same lactic acid bacteria as country buttermilk, but is superior to the latter, because the butter fat has not been removed.

Bacillus Bulgaricus.—*Bacillus bulgaricus*, made famous by the early work and writings of Metchnikoff, is less easily isolated and less constant in milk supplies. It is grown with greater difficulty, requiring incubator temperature and laboratory conditions. It produces from six to eight times more acid than the more common *streptococcus lacticus*, hence it is not suited to making buttermilk. *B. bulgaricus* alone gives too sour a milk and a curd of tenacious consistency. *B. bulgaricus* is therefore adapted only to direct use in the form of tablets and liquid culture.

The commercial preparations are essentially pure cultures of the organism in milk or other suitable medium, made available for use either in a liquid or semi-liquid form, or as dry powders and tablets.

The bacteria are also made available for ingestion in neutral oils and jellies.

These products are marketed in packages suited to the particular character of the output of the several manufacturers for direct use and are rarely, if ever, recommended for making buttermilk.

Bacillus Acidophilus.—*Bacillus acidophilus* is even more elusive than *b. bulgaricus* and is recognized by some authorities as a natural inhabitant of the large intestine. At the present time it occupies the center of the stage by many investigators. It is, however, very significant that large quantities of lactose (milk sugar) are recommended to be given in conjunction with the cultures. Other authorities claim that equally good results follow the ingestion of the lactose alone.

Acidophilus preparations are made by methods similar to those used in the manufacture of *Bulgaricus* preparations and are supplied in much the same forms and packages.

Owing to the comparatively short life of the organism in the dry, semi-solid jellies and oily preparations, the liquid and milk cultures appear to receive most favor. Even then, it is recognized by many users that the liquid products should be used within a week after manufacture.

Rat Virus.—Certain species of bacteria, classified as belonging to the paratyphoid-colon intermediate group of micro organisms, are pathogenic to the common wild rat, field and house mice only, and produce in these rodents a rapidly spreading, highly infectious disease.

The disease is intestinal in character and is spread through soiling of the food with which the diseased rat comes in contact. The normal rats become infected through ingestion of the previously contaminated food, hence when infection becomes established in any locality it extends through that particular colony. A peculiar characteristic of the disease lies in the tendency of the infected animal to seek the open and water, with the result that the animals die away from their burrows and usual haunts. In fact, observers have repeatedly noted that entire areas have been rid of these destructive pests through this tendency. It may be assumed that those resistant members of an infected colony, which do not succumb to their infection, migrate to other localities, thus accounting for the extensive spreading of the malady.

Rat viruses, consisting of live virulent cultures, are produced by several manufacturers and are offered in such forms and packages as will afford convenient means for their distribution as tempting bait to insure their being eaten by the rodents.

The essentials involved in the production of a rat virus include the careful selection and classification of cultures which are pathogenic to these rodents only; the growth of the organism *en masse* in a medium adequately suited to retain the virulence of the organism as well as to provide a palatable bait; and the final packaging of the product to assure that the life and virulence of the organisms are preserved for a sufficient length of time to allow of the economical distribution of the products which usually occurs through the drug trade.

Rat viruses are distributed in various forms, including: pure cultures on a semi-solid medium, with directions to wash the culture from the medium and soak pieces of bread to serve as bait; suspensions of pure cultures in liquid media immediately convenient for distributing on bread, crackers or other attractive bait; and as pure cultures in a dry form to be mixed with cereals or cracker-crumbs and placed in the dry runways.

Before leaving this subject it should be mentioned that a decided difference of opinion exists relative to the safety of rat viruses on account of the possible contamination of food supplies by the infected rodents, and by contact through carrying the bait on the rodents' feet and otherwise. Extensive work has been done to establish the non-pathogenicity to man and other animals of the cultures employed in the manufacture of rat virus, and the danger of such contamination does not exist from the use of those products in which the cultures have been accurately classified and check-tested to establish their identity.

STORAGE OF BIOLOGICAL PRODUCTS

Earlier in this chapter mention was made of the influence of proper storage on the dating, beyond which the manufacturer could not guarantee the activity of his product. The weakening effect of storage at ordinary room temperature, and at even higher temperatures which too often prevail in storerooms, has long been recognized with respect to certain biological products, particularly smallpox vaccine.

Concerted effort on the part of the Federal Government and the manufacturers has been brought to bear, through regulatory measures and caution legends on the labels, to educate the wholesaler, the pharmacist, the physician and others concerned in the handling and storage of biological products, that these commodities, unlike general pharmaceutical preparations, are subject to more or less rapid deterioration, depending on the temperature at which they are stored. Some state legislatures have executed laws, making it compulsory that druggists operating within those states shall provide cold chambers in which to store those biological products which are known to be subject to deterioration.

The manufacturer is very frequently asked to specify those biologicals which should be stored in the cold chamber, and those which may be carried at room temperature. Such differentiation is comparatively simple with respect to smallpox vaccine, the antitoxins, typhoid and paratyphoid vaccines, and those anti bacterial serums on which definite government standards have been adopted, and such other products of bacterial origin on which comparative activity tests may be made in the laboratory. For example, the activity of smallpox vaccine has been shown by laboratory tests on animals to weaken very rapidly when the product is stored at high temperatures, the higher the temperature the more rapid the loss in activity. Conversely the lower the temperature that can be maintained, even to below freezing, the longer the preservation of the activity of the product. Again, repeated tests on serial packages of the antitoxins have provided data upon which a deterioration rate of about 1 per cent per month has been established. Hence a long practical dating is made possible by filling each final container with sufficient excess above the labelled number of units to allow for the above rate of loss.

On the other hand, difference of opinion exists with respect to proper storage of that large group of products of low protein content, in both liquid and dry form, not subject to definite laboratory tests. This group includes the numerous bacterins and bacterial vaccines, spore vaccines, tuberculins, protein extracts and other products in the dry form; and desiccated products of living bacteria. The accumulation of conclusive data, through clinical usage of those bacterial vaccines not subject to laboratory test for activity, presents a problem of considerable proportion. Its solution alone will serve to specify the proper storage for such products.

It is conceded that as new laboratory tests are perfected, with which the rate of deterioration of the yet non-standardized products can be fixed, definite statements as to storage will appear on the respective labels. In the meantime it is a safer procedure to consider all biological products as perishable, and to recommend storage at cold chamber temperature rather than to attempt to differentiate between those for which definite rates of deterioration have been established and those on which scattered data and opinions suggest that cold storage may be unnecessary.

On account of the not infrequent changes in datings, which are authorized by the officials of the U. S. Public Health Service as a result of the compilation of new data on keeping qualities and storage, the datings have been omitted from the description of the products covered in this chapter.

GLOSSARY OF MICROBIOLOGICAL TERMS

- Activity or Activated.**—Capacity for acting; sensibility; vitality; potency; energy. (Gould.)
- Agglutination.**—A phenomenon consisting of the collection into clumps of the cells distributed in a fluid. (Dorland.)
- Agglutinins.**—Substances formed in the blood as a result of infection or immunization which cause adhesion and clumping of the specific bacteria involved in the immunizing process.
- Alexins.**—A defensive protein present in the blood of normal animals. It is synonymous with complement.
- Amboceptor.**—A cytolytic substance supposed to be developed in blood from the injection of foreign cells. It has the power to connect invading cells with complement.
- Anaerobic.**—A term applied to micro-organisms that grow in the absence of free oxygen or air.
- Anaphylaxis.**—The state of excessive susceptibility to the action of a toxin or drug which sometimes follows infection or continued administration of the toxin or drug. (Dorland.)
- Antibody.**—Any one of the constituents of the blood and tissue juices of animals which have been rendered immune by inoculation, and exerting a specific antagonistic influence on the substance under the influence of which it was formed. The antibodies include amboceptors, agglutinins, antienzymes, antitoxins, bacteriolysins, cytotoxins, hemolysins, opsonins and precipitins. (Dorland.)
- Antigens.**—Substances which cause the formation in the animal body of antibodies. The antigens include toxins, ferments, precipitogens, opsogens, agglutinogens, lysogens, antivenins, agglutinins, complements, opsonins, amboceptors, and precipitins.
- Antiseptic.**—An agent which prevents decay or putrefaction by inhibiting the growth of micro-organisms.
- Antitoxin.**—A substance formed in the body of an animal, either naturally or in consequence of inoculation with some pathogenic bacteria, which neutralizes the toxic products of these organisms. (Gould.)
- Asepsis.**—The absence of all micro-organisms.
- Attenuation.**—The thinning or weakening of strength. Attenuation is produced in vaccines, etc., by (a) growing the germs at a temperature above or below the optimum, or (b) by means of a weak antiseptic to reduce their vitality, or (c) by passing the germs through an animal of a different species, or (d) by admixture with an antitoxin or antiserum.
- Autolysate.**—The liquid containing the soluble, toxic, bacterial-cell contents which result from the spontaneous or mechanically induced disintegration of the cell-walls, by which is liberated the unchanged endotoxins into the surrounding medium.
- Bacterins.**—Bacterial vaccines.
- Complement.**—A ferment-like body existing normally in cell protoplasm. It acts in conjunction with the amboceptor, for action on invading cells. It is destroyed by heating to 56–60° C. for 30

- minutes, at which temperature the amboceptor is not destroyed. (Wassermann reaction.)
- Contagion.**—The communication of disease by direct or indirect contact.
- Culture Media.**—Substances used for cultivating bacteria, and on or in which they grow.
- Desensitizing.**—Depriving of sensation, decreasing or removing the anaphylactic sensitiveness.
- Desensitization.**—A condition in which the organism is rendered very insensitive to a specific protein. (Dorland.)
- Diagnostic.**—Determining or confirming a diagnosis; serving as sufficient evidence in a diagnosis.
- Disinfectant.**—An agent which destroys disease-producing organisms.
- Endotoxins.**—Toxins which do not diffuse through the cell-walls—intracellular toxins, germs, ferments, etc.
- Erythrocytes.**—Red blood corpuscles.
- Etiological.**—Pertaining to etiology or to the causes of disease.
- Extracellular.**—Outside of a cell or cells. (Dorland.)
- Flora.**—The entire bacterial content of any area.
- Fixed Virus.**—A virus of definite strength. (See Virus.)
- Globulins.**—Proteins which are insoluble in water but soluble in physiological salt solution. Specifically, purified antitoxins.
- Haptophile.**—Having a peculiar affinity for a haptophore. (Dorland.)
- Haptophore.**—The stable, non-poisonous element of a toxin which enables it to unite with an antitoxin and become neutralized. (Dorland.) (Ehrlich's side-chain theory.)
- Hemolysis.**—The destruction of the blood corpuscles (usually the red corpuscles) by specific lysins.
- Homologous.**—Of similar structure or situation, but not necessarily of similar function. (Dorland.)
- Hyperimmune.**—Denoting a higher degree of immunity than that which occurs from natural infection.
- Hyperimmunizing.**—Introducing organisms into the body beyond the point of establishment of immunity.
- Immunity.**—Exemption from or resistance to disease. Usually applied as to specific diseases. Immunity may be **natural** or **acquired**. Acquired immunity is **active** when it results from infection and recovery, or from vaccines, or **passive** when it is produced temporarily by antitoxins.
- Immunity Unit (Antitoxin Unit).**—A unit for expressing the strength of an antitoxin. The unit of diphtheria antitoxin is approximately the amount of antitoxin which will preserve the life of a guinea pig weighing 250 Gm. for at least four days after it is injected subcutaneously with a mixture of 100 times the minimum fatal dose of diphtheria toxin and the antitoxin. (Dorland.)
- Immunization.**—The process of rendering a subject immune, or of becoming immune. (Dorland.)
- Incubation.**—The development of bacteria, or the period between infection and the first symptoms of disease.
- Infection.**—The communication of disease germs by any means.
- Inoculation.**—The introduction of the germs or virus of a disease into the body.

- Intracellular.**—Situating or occurring within a cell or cells. (Dorland.)
- Intracutaneous.**—Within the substance of the skin. (Dorland.)
- Intradermal.**—Situating or applied within the skin. (Dorland.)
- Intramuscular.**—Situating in the substance of a muscle. (Dorland.)
- Intrapalpebral.**—Situating or occurring within the eyelid.
- Intraspinal.**—Situating in the substance of the spinal column. (Dorland.)
- Intravenous.**—In, into, or from within a vein or veins. (Dorland.)
- Lethal.**—Deadly, fatal. (Dorland.)
- Leucocytes.**—White blood corpuscles.
- Lysins.**—An antibody which causes dissolution of cells.
- Bacteriolysins.**—Dissolve and destroy bacteria.
- Hemolysins.**—Dissolve red blood corpuscles.
- Cytolysins.**—Destroy and dissolve cells.
- L+ Dose.**—The smallest amount of diphtheria toxin which will kill a 250 Gm. guinea pig within four days when mixed with one unit of diphtheria antitoxin before being injected subcutaneously. (Dorland.)
- M. L. D.**—Minimum Lethal Dose. The smallest quantity of toxic material that will cause death within a certain length of time.
- Mycological.**—Pertaining to the science and study of fungi.
- Non-specific.**—Not having a specific function.
- Opsinogens.**—Vaccines. Substances which develop opsonins.
- Opsonins.**—Indefinite elements in the blood which act on invading bacteria in such a way that they become easy prey to the phagocytes. There appears to be specific opsonins for specific bacteria.
- Opsonic Index.**—The measure, or relative amount, of opsonins in an individual. Usually a comparison of a diseased person's resistance with that of a healthy person.
- Opsonic Therapy.**—Treatment by means of vaccines.
- Parenteral.**—Not through the alimentary canal, *i. e.*, either subcutaneous or intravenous. (Dorland.)
- Pathogenic.**—Disease producing.
- Phagocytes.**—A white blood cell, or other cell, having the power to ingest bacteria.
- Phagocytosis.**—The destruction of bacteria within the body by the action of phagocytes.
- Potency.**—As applied to serums, the power of a serum to neutralize its homologous toxin.
- Polyvalent.**—As applied to biological products, it refers to a combined action of two or more strains or species.
- Precipitins.**—Substances formed in the blood or other body fluids which cause precipitation of specific bacteria or of other bodies when mixed with fluids containing proteids of a foreign character. Used forensically to determine the source of a blood.
- Prophylactic.**—Disease preventing. An agent which prevents or wards off disease.
- Pseudoglobulin.**—One of the two proteins (the other being euglobulin) of which globulin consists. It is characterized by not being precipitated by dialysis. (Dorland.)
- Receptors.**—Supposed groups of atoms of the cell molecule which have the power of combining with and anchoring the haptophore groups

of toxins, of amboceptors or of cells. Receptors may remain attached to the cell, or may be cast off into the serum. In either case they retain their combining powers. (Dorland.)

Saprophytic Bacteria.—Bacteria which can grow and reproduce on dead matter.

Serological.—Pertaining to sera and the study of sera. (Dorland.)

Serum.—The colorless and non-coagulable fluid of blood.

Specific.—Pertaining to a species. Produced by a single kind of micro-organisms. A remedy specially indicated for any particular disease. (Dorland.)

S. T. D.—Skin Test Dose. The smallest amount of toxin that will produce a definite skin reaction, when injected intracutaneously into susceptible individuals, within a definite period of time.

Subcutaneous.—Situating or occurring beneath the skin. (Dorland.)

Symbiosis.—The dependence of one organism upon another for growth and development.

Titre.—A suffix signifying the measure of, *e. g.*, *colontitre* is the smallest amount of a certain substance which indicates the presence of colon bacillus. *Agglutination titre*, the highest dilution of a serum which causes clumping of bacteria. (Dorland.)

Toxins.—Bodies of unknown chemical composition, produced by bacterial action, and probably resembling enzymes, having powerful poisonous qualities.

Phytotoxins.—Toxins derived from plants.

Zootoxins.—Animal toxins. Venoms.

Microbial Toxins.—Toxins from bacteria.

Endotoxins.—Toxins secreted within the bodies of the bacteria.

Soluble Toxins.—Toxins excreted by the growing bacteria and dissolved in the media. Also toxins found in serums, venoms, etc.

Toxophore.—The second combining group of toxins, which is easily destroyed by heat. (Ehrlich's side-chain theory.)

Vaccines.—Attenuated or modified viruses.

Autogenous Vaccines.—Bacterial vaccines prepared from cultures taken from the patient to be treated.

Bacterial Vaccines.—Suspensions of dead bacteria in physiological salt solution, or in bouillon.

Personal Vaccines.—Same as autogenous vaccines.

Stock Vaccines.—Bacterial vaccines prepared from the proper bacteria and standardized to contain a definite number of dead bacteria.

Virulent.—Exceedingly infectious, noxious or deleterious.

Virus.—The poison or contagium of an infectious disease.

Filtrable Virus.—A virus which can pass through supposedly germ-proof filters. Filterable viruses probably contain organisms too small to be removed by filtration or be recognized in the microscope.

Fixed Virus.—A virus of known potency. A vaccine virus.

LIST OF LICENSED BIOLOGICAL PRODUCTS FOR USE ON HUMANS

Animal food extract
 Animal epidermal extract
 Antianthrax serum
 Antidysenteric serum
 Antigonococcic serum
 Antimelitensis serum
 Antimeningococcic serum
 Antiplague serum
 Antipneumococcic serum
 Antistreptococcic serum

Bacterial vaccines made from,
 acne bacillus
 acne diplococcus
 cholera vibrio
 colon bacillus
 dysentery bacillus
 enterococcus
 Friedlander bacillus
 gonococcus
 influenza bacillus
 meningococcus
 micrococcus catarrhalis
 micrococcus melitensis
 micrococcus tetragenus
 nonvirulent tubercle bacillus
 paratyphoid bacillus A
 paratyphoid bacillus B
 pertussis bacillus
 plague bacillus
 pneumococcus
 prodigiosus bacillus
 pseudodiphtheria bacillus
 staphylococcus albus
 staphylococcus aureus
 staphylococcus citreus
 streptococcus
 synococcus
 typhoid bacillus

Bacterial Antigens made from
 gonococcus
 pertussis bacillus
 pneumococcus
 staphylococcus
 streptococcus

Botulinus antitoxin

Diphtheria antitoxin
 Diphtheria toxin for Schick test
 Diphtheria toxin-antitoxin mixture

Hemostatic serum (LaPenta), Hemoplastin.

Leucocytic extract from the horse

Measles immune serum
 Modified bacterial derivatives
 colon bacillus
 gonococcus
 paratyphoid bacillus A
 paratyphoid bacillus B
 pneumococcus

staphylococcus albus
staphylococcus aureus
streptococcus
typhoid bacillus
Modified tubercle bacillus derivatives (von Ruck)

Normal horse serum

Perfringens antitoxin
Pneumococcus antibody solution
Poison ivy extract
Pollen extract

Rabies vaccine (Cumming)
Rabies vaccine (dilution method)
Rabies vaccine (Harris)
Rabies vaccine (killed virus)
Rabies vaccine (Pasteur)

Scarlet fever streptococcus antitoxin
Scarlet fever streptococcus toxin for Dick test
Scarlet fever streptococcus toxin for immunization
Sensitized bacterial vaccines made from

acne bacillus
cholera vibrio
colon bacillus
Friedlander bacillus
gonococcus
influenza bacillus
meningococcus
micrococcus catarrhalis
paratyphoid bacillus A
paratyphoid bacillus B
pertussis bacillus
pneumococcus
pseudodiphtheria bacillus
staphylococcus albus
staphylococcus aureus
streptococcus
typhoid bacillus

Tetanus antitoxin
Thyroidectomized horse serum
Tuberculin B.E.
Tuberculin B.F.
Tuberculin ointment (Moro)
Tuberculin old
Tuberculin proteose-free (Lyons)
Tuberculin T.R.

Vaccine virus
Vegetable food extract

Watery extract of tubercle bacilli (von Ruck)

LIST OF REPRESENTATIVE BIOLOGICAL PRODUCTS FOR USE ON DOMESTIC ANIMALS

Anti-anthrax serum
Anti-blackleg serum
Anti-bovine abortion serum
Anti-distemper serum (canine)
Anti-equine abortion serum
Anti-hemorrhagic septicemia serum

Anti-influenza serum (equine)
Anti-streptococcic serum (equine)
Anti-white scour (anti-calf scour) serum (bovine)
Anti-hog cholera serum
Anti-mixed infection serum (for swine)
Anti-pig dysentery serum
Anti-mixed infection serum (avian)
Anti-navel ill serum (equine)
Anti-swine erysipelas serum
Anthrax vaccine
Autogenous bacterin
Abortion bacterin (equine)
Abortion bacterin (bovine)
Abortion vaccine (bovine)
Abortion bacterin mixed (bovine)
Abortion bacterin mixed (equine)
Abortion bacterin mixed (swine)
Anthrax aggressin

Blackleg aggressin
Blackleg filtrate
Blackleg vaccine
Blackleg bacterin
Botulinus antitoxin
Bovine abortion serobacterin
Bovine abortion serovaccine
Bacillus suispestifer bacterin

Canine distemper antigen
Canine distemper bacterin
Canine distemper mixed bacterin
Canine distemper serobacterin
Canine distemper serobacterin, mixed
Colon bacterin (equine)
Colon bacterin (bovine)
Chicken pox vaccine
Chicken pox virus
Calf scour mixed bacterin

Distemper mixed bacterin for horses

Equine Abortion Serobacterin, Mixed
Equine Influenza Bacterin
Equine Influenza Mixed Bacterin
Equine Influenza Serobacterin, Mixed
Equine Navel Ill Serobacterin, Mixed
Equine Staphylococcus aureus and albus Bacterin
Endometritis Mixed Bacterin (bovine and equine)

Fowl Cholera Bacterin
Fowl Typhoid Mixed Bacterin
Fowl Typhoid Bacterin
Fowl Typhoid and Fowl Cholera Mixed Bacterin

Gastroenteritis Mixed Bacterin (equine)

Hemorrhagic Septicemia Aggressin
Hemorrhagic Septicemia Bacterin
Hemorrhagic Septicemia Vaccine
Hemorrhagic Septicemia and Infectious Enteritis Mixed Bacterin (for swine)
Hog Cholera Virus

Infectious Rhinitis Mixed Bacterin (for swine)

Keratitis Mixed Bacterin, bovine

- The Abbott Laboratories, 4735 East Ravenswood Avenue, Chicago, Ill.—License No. 43.
- Dr. W. T. McDougall, 640 Minnesota Avenue, Kansas City, Kans.—License No. 49.
- St. Louis Pasteur Institute, 3514 Lucas Avenue, St. Louis, Mo.—License No. 50.
- The Upjohn Co., Kalamazoo, Mich.—License No. 51.
- E. R. Squibb & Sons' Research and Biological Laboratories, New Brunswick, N. J.—License No. 52.
- Laboratory of Clinical Pathology, Thirty-first Street and Troost Avenue, Kansas City, Mo.—License No. 53.
- Dr. James McL. Phillips, 2057 North High Street, Columbus, Ohio.—License No. 54.
- Eli Lilly & Co., Indianapolis, Ind.—License No. 56.
- Swan, Myers Co., 219 North Senate Avenue, Indianapolis, Ind.—License No. 58.
- Gilliland Laboratories, Marietta, Pa.—License No. 63.
- Antitoxin and Vaccine Laboratory, Department of Public Health, Commonwealth of Massachusetts, Jamaica Plain, Boston 30, Mass.—License No. 64.
- United States Standard Products Co., Woodworth, Wis.—License No. 65.
- D. L. Harris Laboratories, Metropolitan Building, St. Louis, Mo.—License No. 66.
- The Arlington Chemical Co., Yonkers, N. Y.—License No. 67.
- Dermatological Research Laboratories, Philadelphia, Pa. (Branch of Abbott Laboratories, Chicago, Ill.)—License No. 68.
- H. A. Metz Laboratories, 122 Hudson Street, New York City.—License No. 69.
- Synthetic Drugs and Diarsenol Laboratories, Buffalo, N. Y.—License No. 70.
- Hynson, Westcott & Dunning, Baltimore, Md.—License No. 76.
- Mallinckrodt Chemical Works, St. Louis, Mo.—License No. 77.
- Agricultural Experiment Station, College of Agriculture, University of Illinois, Urbana, Ill.—License No. 81.
- Powers-Weightman-Rosengarten Co., Philadelphia, Pa.—License No. 82.
- Terrell Laboratories, 311 State Bank Building, Fort Worth, Tex.—License No. 84.
- Jensen-Salsbury Laboratories, Kansas City, Mo.—License No. 85.
- Cook Laboratories, 536 Lake Shore Drive, Chicago, Ill.—License No. 86.
- The Neosol Co., 72 Kingsley St., Buffalo, N. Y.—License No. 90.
- Hollister-Stier Laboratories, 312 Old National Bank Bldg., Spokane, Washington.—License No. 91.
- DePree Laboratories, Holland, Michigan.—License No. 93.
- The Jackson Infirmary, Jackson, Mississippi.—License No. 96.

MANUFACTURERS LOCATED IN OTHER COUNTRIES

- Institut Pasteur de Paris, Paris, France.—License No. 11. Selling agents for the United States. Pasteur Laboratories of America, 366 West Eleventh Street, New York City.

- Farbwerke Hoechst, vorm. Meister Lucius and Brüning, Hoechst am Main, Germany.—License No. 24. Selling agents for the United States. H. A. Metz Laboratories, 122 Hudson St., New York City.
- E. Merck, Darmstadt, Germany.—License No. 31. Selling agents for the United States. Merck & Co., 45-47 Park Place, New York City.
- Connaught Antitoxin Laboratory, University of Toronto, Canada.—License No. 73.
- Les Etablissements Poulenc Freres, 92 Rue Vicille-du Temple, Paris, III, France.—License No. 74. Selling agents for the United States. Geo. J. Wallau, 6 Cliff St., New York City.
- Laboratoire de Biochimie Medicale, 92 Rue Michel-Ange, Paris, France.—License No. 83. Selling agents for the United States: Anglo-French Drug Co., 1270 Broadway, New York City. Selling agents for Porto Rico: Chas. Vere, Box 216, San Juan, P. R.
- Instituto Sieroterapico Milanese, Milan, Italy.—License No. 87. Selling agents for the United States: Neother Products Co., 50 Union Square, New York City.
- Institut National de Vaccinothérapie, 26 Rue Pages, Suresnes (Seine) near Paris, France.—License No. 95.
- Behringswerke, A. G., Marburg-am-Lahn, Germany.—License No. 97.

CHAPTER XVII

HOMEOPATHIC PHARMACY

The word homeopathy comes from the Greek words *ὅμοιος*, like or similar, and *πάθος*, suffering, and refers to the fundamental doctrine of this form of practice, that "like cures like." It was founded by Samuel Hahnemann, a German physician, born at Meissen, near Dresden, in Saxony, who was led by the marked effect of a large dose of cinchona to adopt the principle that a remedy given to a healthy subject should produce the symptoms of the disease it would cure. He tried many remedies, and embodied his researches in two extensive volumes. Most of the principles of homeopathic pharmacy and practice were set forth by him in the latter part of the eighteenth century, and but few changes have been made since that time.

The principal motto of the system, "*similia similibus curantur*"—like cures like—while first applied to modern medicine by Dr. Hahnemann, is yet very old, for Antiphanes says, 404 B. C.:

"Take the hair, it is well written,
Of the dog by which you're bitten;
Work off one wine by his brother
And one labor with another;
Cook with cook, and strife with strife,
Business with business, and wife with wife."

Homeopathic Pharmacy was first practiced in Leipsic in 1775, and is thus comparatively new. The main principles at present advocated are: 1st. All medicines must be proved by administration to subjects in health. 2d. Remedies should be given alone, not in combination. 3d. Insoluble substances become very active medicinal agents after being reduced to an impalpable powder and thoroughly diffused through some inert substance. 4th. All medicines should be given in doses too small to produce their physiological effects.

We find no mixtures in homeopathic pharmacy. Two remedies are sometimes given alternately, but never or very seldom mixed. Remedies are also given in very small doses, since they are supposed to act upon a principle directly opposite to that adopted in allopathic practice.

The number of remedies used was originally about two hundred, but now reaches nearly a thousand. Among these are vegetable drugs, chemicals, and a large number of animal drugs, insects, etc., including musk, cantharides, burnt sponge, honey bees, cuttle-fish ink, crab, certain species of spider, several reptile poisons, star-fish, bed-bugs, cockroaches, etc.

With a few exceptions, as nux vomica, rhubarb and cinchona, the drugs are used and preparations made from them while fresh and undried, and animals and insects are captured and preserved alive

until the moment of use. The nomenclature differs from that of our Pharmacopœia, being adapted largely from the German. Thus cinchona is called "china;" quinine, "chininum;" wormseed, "cina;" calomel, "mercurius dulcis;" and mercury, "mercurius vivus," etc.

Great stress is laid upon the purity and strength of all drugs and preparations.

Thus, only distilled water is used, and that required to be obtained from tin-lined stills and condensers which are used for no other liquids. Alcohol is required to be re-distilled and kept in glass containers.

Sugar of milk is directed to be purified by recrystallizing or by precipitating with alcohol.

Homeopathic pharmacopœias have been published in England and Germany, and a National American Homeopathic Pharmacopœia has been issued which is authorized and published by a committee appointed for that purpose, and corresponds to the United States Pharmacopœia.

The English Pharmacopœia, and an American Pharmacopœia, published independently by Boerick & Tafel, had been previously employed by American practitioners.

Homeopathic preparations are of three classes, (1) the tinctures, commonly called "mother tinctures," which are solutions of the soluble principles of drugs in alcohol, mixtures of alcohol and water, or, rarely, in ether, glycerin or syrup; (2) liquid attenuations made from these; and (3) powders, usually in the form of triturations.

Infusions and decoctions are used but rarely, and are made in the usual way.

Cold infusions are made by percolation, and hot infusions by maceration. All are filtered after being strained, and are made of a uniform strength—10 per cent.

The mother tinctures are also made of a uniform strength—10 per cent—based on the *dry* drug, and great pains are taken to have the alcoholic strength the same in all cases, for the same drug. Since these are made from fresh drugs, the amount of moisture must be estimated in each lot, and allowance made for it. Thus, if tincture of aconite is to be made, using 50 per cent alcohol as a menstruum, the amount of moisture is first estimated, and enough strong alcohol added to make 50 per cent alcohol with the natural juice of the root. Supposing that it contains 70 per cent of moisture; there is first poured upon 4 troy ounces of the drug, packed in the percolator, 3.27 fluidounces (wine measure) of 90 per cent alcohol, the amount necessary for the conversion of the water in the drug into 50 per cent alcohol. This is followed with menstruum of the required strength.

Most tinctures are made by percolation in glass apparatus, and those which are affected by light are stored in yellow (or amber) glass bottles. The drugs are never milled, but are prepared for percolation by bruising to a pulp in a Wedgwood mortar. Fibrous drugs are first cut in a tinned-iron mincing machine.

They are never allowed to come in contact with metal other than polished or tinned-iron.

Chemical bodies which are soluble are sometimes used in solution, alcohol, glycerin, ether, or syrup being used as a solvent. They

are required to be clear and bright in all cases, and in case of change of character on keeping, are to be rejected.

These 10 per cent tinctures or solutions are seldom administered as made, but in nearly all cases are diluted.

The dilutions are all made in decimal proportion, and are termed *dilutions*, *attenuations*, or (rarely) *potencies*.

The tinctures or chemicals are designated by the sign θ or Φ , the word tincture or solution not being employed in prescriptions. Thus "aconitum Φ " means "mother tincture of aconite;" "acid nitricum Φ " means 10 per cent solution of nitric acid.

The dilutions are of two grades, the *decimal* and the *centesimal*. The former are denoted by numbers followed by X, and usually only the odd numbers are employed, since, the even numbers will correspond to the centesimal dilutions, as 1^x , 3^x , 5^x , 7^x , etc. (2^x would correspond to the first centesimal dilution, 4^x to the second, etc.).

The centesimal dilutions are designated by simple numbers, as 1, 2, 3, 4, 5, etc.

The decimal dilutions are made by placing 10 minims of the mother tincture in a bottle and adding to it 90 minims of spirit of the same strength as the menstruum in the tincture. This is shaken with several jerks of the arm, and constitutes the first dilution, 1^x . The second dilution is made in the same way, using 1^x in place of Φ , and the mixture then constitutes the second dilution. For the fourth dilution, and all thereafter, strong alcohol is used. The second dilution is usually made with an alcohol intermediate in strength between that of the menstruum and strong alcohol.

The centesimal dilutions are made by shaking 1 minim of mother tincture with 99 minims of menstruum, this making the first centesimal dilution, or 2^x , or 1.

The second is made in like manner, using 1 minim of the first and 99 minims of the spirit.

Like the decimal dilutions, all the centesimal dilutions after the second are made with strong alcohol.

Both the decimal and centesimal dilutions can be carried up to the thousandths, and the thirty-thousandth dilution has been called for, but usually the third decimal or the sixth or thirtieth centesimal dilution is called for.

The bottles in which these or the mother tinctures, solutions, etc., are kept should be cleansed, then rinsed with distilled water, and never used for any other variety. The diluting should be done in diffused, not in direct sunlight.

Triturations are mixtures of medicinal substances with sugar of milk. The medicinal substance is in most cases a chemical or insoluble body, but occasionally triturations are made by absorbing tinctures or dilutions in sugar of milk. The object of triturations is not only to diffuse and dilute the medicinal substances, but also, by long trituration, to subdivide it into the finest possible powder. Consequently a simple mixing, as by means of a sieve, will not suffice, but the two must be triturated together.

Sugar of milk is selected as a base because (1) it is devoid of medicinal action, and (2) because its crystals are very hard and of use in grinding the substance.

Wedgwood or porcelain mortars, and spatulas of bone, horn or glass, are directed to be used in making triturations.

The triturations correspond in strength to the dilutions, being of decimal or centesimal strength. The medicinal substance and the sugar of milk should both be in fine powder before mixing. If sifting is necessary, a sieve made of hair cloth is directed.

To make the first decimal trituration, the substance is placed in a clean Wedgwood mortar, and an equal weight of sugar of milk is added. These are first mixed by stirring with a glass spatula for a few moments, then they are triturated with force for six minutes, after which four minutes are occupied with scraping the powder from the sides of the mortar and pestle and mixing with the spatula, and then the trituration and scraping are repeated.

Then three parts (or three times the original weight) more of sugar of milk are added and triturated in the same way for twenty minutes, and finally five parts more of sugar of milk are poured in and triturated twenty minutes. An hour is thus occupied in making the first decimal trituration, but since most of the grinding action will necessarily be brought to bear upon the drug in making this, only half an hour is required in making each succeeding trituration. The sugar of milk is added in three portions as at first, each portion being triturated ten minutes.

The centesimal triturations are made preferably from the decimal, or at least from the first decimal trituration.

In making triturations, it is recommended that a separate or special mortar be used for each kind, since the power is extended from the remedy to the mortar. Where this cannot be done, it is required that the mortar be first cleansed thoroughly, then purified by burning alcohol in it.

If triturations are made in the drug stores, a Wedgwood mortar and pestle should be set aside for this work alone, so that those which are used for general work will not be used also for this.

Homeopathic remedies are dispensed in powders, attenuations and globules.

Rarely the tinctures are dispensed and directed to be added to a definite amount of water, of which a teaspoonful or a certain number of drops are to be taken.

The powders consist of sugar of milk, to which a given quantity of a trituration or of a dilution or tincture is added.

If the latter is used, it must be remembered that a weak alcohol will soften and partially dissolve the sugar of milk. Tincture triturations are sometimes made of which one grain corresponds to one minim of tincture.

The powders may be divided and dispensed in papers in the usual way.

The globules or pellets are little pilules of cane sugar, which are used as vehicles for the dilutions, in this providing for the administrations of fractions of a drop.

They come of various sizes, designated by numbers, the latter corresponding to the number of millimeters which ten pellets measure when placed in a row.

They are medicated by filling a vial loosely with the pellets, then pouring over them the required attenuation.

The 3rd or higher dilution is commonly used. After standing a few minutes to allow of absorption, the liquid is drained off and the pellets allowed to dry.

In some sections it is customary to dispense them with a portion of the liquid in the bottle, the pellets, of course, being undried. It is stated that a 75 per cent alcohol absorbs better than 90 per cent, and in some cases the globules are directed to be moistened with water before adding the alcoholic solution, to facilitate absorption.

It is largely for the purpose of medicating globules, however, that dilutions are made with alcohol instead of water.

Homeopathic prescriptions are usually abbreviated to an extreme, the nomenclature allowing of this without ambiguity. The strength of preparation usually follows the name, and after this the quantity.

The strength and quantity may also be written in fraction form, the numerator then corresponding to the quantity, and the denominator to the strength, as

R. Ferri Mur.....	3 ^x gtt. vj.	
Aquæ Destill.....	3ij.	M. Or
R. Tinct. Ferri Mur.....	$\frac{3^x}{3}$	
Aquæ Destill.....	3ij.	M.

Six drops of the third decimal dilution of tincture of muriate of iron are to be diluted with two fluidounces of distilled water.

R. Aconiti.....	gtt. $\frac{3}{3}$.	
Aquæ Dest.....	3vj.	M. Or
R. Tinct. Aconiti.....	3 gtt. iij.	
Aquæ Destillat.....	3vj.	M.

Three drops of the third centesimal dilution of tincture of aconite are to be added to six fluidounces of distilled water.

R. Trit. Natr. Mur.....	30 gr. xij.	
Sacchar. Lactis.....	q. s.	
M. ft. pulv.....	xij no.	Or
R. Nat. Mur.....	gr. $\frac{12}{30}$.	
Sacchar. Lactis.....	q. s.	
M. ft. pulv.....	xij no.	

Twelve grains of the thirtieth centesimal dilution of sodium chloride are to be mixed with sufficient sugar of milk and divided into twelve powders.

R. Pil. Nux V.....	$\frac{50}{12}$.	Or
R. Nux V.....	12, pil.	L.

Fifty pills (or globules) of the twelfth centesimal dilution are desired.

R. Tinct. Bellad.....	θ gtt. ij.	
Aquæ Destill.....	3iv.	M.

Two drops of mother-tincture of belladonna are to be added to four fluidounces of distilled water.

R. (1) Sulph..... $\frac{2}{30}$ Nos. 1-11.
 (2) Sulph..... $\frac{2}{200}$ Nos. 2-12.
 Mitte tales pulv..... xij no.

Sig.—A powder night and morning in a wineglassful of water.

This calls for (1) 6 powders of the 30th dilution of sulphur, 2 grains each numbered 1 to 11 (1, 3, 5, 7, 9, and 11) and (2) also 6 powders of the 200th dilution, 2 grains each, numbered 2 to 12 (2, 4, 6, 8, 10, 12). The powders are to be taken in numerical order.

Whatever may be thought of homeopathic remedies and methods, the pharmacist who accepts prescriptions from homeopathic physicians owes it as much to them as to any to prepare such, as far as lies in his power, in accordance with the ideas and wishes of the prescribers.

CHAPTER XVIII

INCOMPATIBILITY

The subject of incompatibility is an exceedingly broad and deep one. It means an intimate knowledge of chemical physics and chemical reactions, and since these are constantly being increased, the question of incompatibilities can be said to have no end. As long as pharmacy exists there will be something to learn in this line, and no man can be considered to know it all. There is, however, a great difference between *possible* and *probable* incompatibilities, and the study of the latter is not a formidable one, "if there exists primarily a clear knowledge of the chemical and pharmaceutical properties of the substances used." The best and easiest method of acquainting one's self with the general subject of chemical incompatibility is by a study of qualitative analysis, and it is chiefly for this reason that this subject is taught in colleges of pharmacy. After a course in qualitative analysis, and a systematic study of the official preparations and processes, the student possesses a foundation upon which quite a clear understanding of the usual incompatibilities may be based.

Success at the prescription counter rests very largely upon a correct application of the principles included in these. In no way can the pharmacist be as helpful to the physician as in the correction of incompatibilities, and it were well if every retail pharmacist could have an understanding with the physicians in his vicinity that prescriptions which can be improved without (*positively*) any alteration in medicinal properties, should be so treated by the pharmacist, and full notes of such changes sent immediately to the physician, either by mail or with the medicine to the house of the patient. It should be noted, however, that any study of this sort means not only a study of incompatibilities, but also of the *means of overcoming them*. The physician, like other people, does not like to be told what he *cannot or must not* do; he wishes to know what he *can* do, and if improvements are to be made, he is usually ready to listen.

This phase of the situation is too often neglected by retail pharmacists, to the advantage and profit of the manufacturer, who makes it his chief aim to produce elegant and presentable combinations, which the physicians desire.

Therefore, *study first to know the incompatibilities, and second, (more assiduously) to know how they may be overcome*. The following notes are arranged with this object in view.

Incompatibilities are of three kinds: therapeutical, pharmaceutical and chemical.

THERAPEUTICAL INCOMPATIBILITIES

Therapeutical incompatibilities are those in which drugs are combined, which act contrary to each other upon the system. This is

purely a question of the medicinal action of drugs, and is beyond the ken of pharmacists. Unless it is obvious that the physician has written absent-mindedly, and ordered combinations which can scarcely be desirable under any circumstances, *or has prescribed dangerous doses*, the question of action should never be raised by the pharmacist in order to correct.

The chief concern of the pharmacist on the therapeutic line is the safety of the patient and he must be constantly alert to detect excessive or dangerous doses in prescriptions.

It is well also to remember that antagonistic remedies may be purposely prescribed together, one acting perhaps as a corrective of the other. This is a condition which is found oftentimes in nature, as in rhubarb, which contains both a cathartic and an astringent principle; in digitalis, which contains certain principles which powerfully contract the arteries, and another which dilates them; and in jaborandi, opium and many other drugs, which contain antagonistic principles, but in such proportions that one does not neutralize another, but only modifies or corrects its action.

The pharmacist should never attempt to judge the physician in these matters, but *should ever be on the alert for unusual and dangerous doses or combinations*. It is for the physician to excel in the details of therapeutics, and for the pharmacist to excel in the details of chemistry and physics.

PHARMACEUTICAL INCOMPATIBILITIES

Pharmaceutical, or physical, incompatibilities are **chiefly cases of insolubility**, as when a body which should be administered in solution is insoluble in the combined ingredients of the mixture, or when a body already dissolved is thrown out of solution by admixture with other bodies. Bodies which are insoluble in the ordinary solvents are not considered incompatible in this sense, unless the nature of the mixture is such that an even diffusion of the insoluble substance cannot be readily obtained.

The larger proportion of pharmaceutical incompatibilities can be remedied by changes in the solvent or by some protective or suspending agent. A clear solution cannot always be obtained, but this may not be necessary when a homogeneous mixture, which can be depended upon to yield an even dose each time of all ingredients, is secured. The treatment of these calls for an intimate knowledge of the solubility of all the common remedies in the ordinary solvents, which can only be learned gradually. It affords an interesting and profitable field for study, which is never-ending, yet not discouraging, and is, moreover, a direct means of success to a pharmacist in many cases.

Among the most common illustrations of physical incompatibilities are:

(a) Mixtures of alcoholic tinctures, fluid extracts, etc., with aqueous fluids, the dissolved drug-principles being thrown out of solution.

(b) Solutions of metallic salts in aromatic waters, the aromatic oil being thrown out of solution; or solutions of salts in hydro-alcoholic liquids, the salt or the alcohol being separated.

(c) Supersaturated solutions which should not be filtered.

(d) Mucilaginous and albuminous bodies with strong alcoholic liquids.

There are four general methods of remedying or preventing physical incompatibilities:

- (1) By the order of mixing.
- (2) By changes in the bulk of the mixture, whereby the alcoholic or solution strength is kept within certain limits.
- (3) By alterations in the solvents used.
- (4) By emulsifying or suspending the troublesome body with gums or syrups.

1. **The order of mixing** has much to do with the final appearance of the mixture. When a prescription is received, the first thought of the dispenser should be, "In what order should these be mixed?" Oftentimes two ingredients, which alone are incompatible, can be made presentable by first mixing one or both with other ingredients of the mixture. It is always easier to *prevent* precipitation or ill appearance than to remedy it, and the order of mixing oftentimes avails in this way. When a mixture calls for a strong alcoholic liquid to be mixed with weaker alcoholic fluids and water, the strongly alcoholic liquid should be gradually diluted with the weaker, and the water added last. By this procedure a less voluminous precipitation occurs.

If a resinous tincture is to be mixed with water, no protective agent being allowable, *the water should be cold and the tincture added to it* in a fine stream, not *vice versa*. The resinous matters are thus precipitated in a fine condition, and easily diffuse upon shaking. Compound tincture of benzoin, and tincture of myrrh are frequently prescribed in this way. Camphoraceous solutions should also be added to the water, unless other bodies are present which will prevent their separation, when the solution is protected by this before being mixed with water.

2. **Changes in the Total Bulk of the Mixture.**—The alcoholic strength of a mixture frequently determines whether a salt shall remain in solution or not, and contrariwise the presence of a salt in large proportion, which is soluble in water but insoluble in alcohol, may prevent the mixing of alcoholic fluids.

The alkaloids in certain combinations are the most frequent cases of the first kind. Strychnine in combination with bromides, iodides, and other metallic salts, requires the presence of at least 12 per cent of alcohol to hold it in solution. In such cases it is not the *amount* of alcohol present which holds the salt in solution, but the *proportion or percentage* strength of the mixture; hence the problem is simply to keep the alcoholic strength of the mixture up to that necessary for complete solution. When alcoholic liquids are combined with water, this is best accomplished, not by adding alcohol, but by reducing the quantity of water so that the finished solution measures just half of that originally intended, the dose being changed accordingly.

In the opposite class, when a concentrated solution of a salt throws out of solution a salt which is commonly soluble in water, the simplest remedy is to double the measure of the mixture by addition of water, the dose also being doubled. No. 11 (p. 442) illustrates this. *But such changes in the volumes and doses of prescriptions should never be made without the knowledge and consent of the physician.*

Suggestions for diluting might also be made to the patient whenever it is judged that such will be received intelligently, and without reflection upon the prescriber.

In cases of supersaturated solutions, the insoluble body should be powdered finely, so that agitation will diffuse it evenly throughout the liquid. Never use heat to dissolve the excess of salt, and do not filter.

3. **By alterations in the solvents or by protective agents.**—This requires a pretty thorough knowledge of the comparative value of the different solvents upon the different principles, salts, etc., when in combination. This means something more than the question whether the body is soluble in so many parts of such and such a solvent; it means also the question whether certain *solutions* can be combined without precipitating one of the dissolved bodies.

Water is the great solvent, but aqueous solutions of some salts may not be miscible with alcohol without separation either of the salt or of the alcohol. Much also depends upon the *strength* as well as the *nature* of the solutions, weak solutions often being miscible when strong ones are not.

The chief solvents to be considered in this connection are water, alcohol and glycerin.

Water dissolves gums, albuminous bodies, mucilages, and proteins, but these solutions are not miscible with alcohol unless dilute. It dissolves many salts, some of which are precipitated on addition of alcohol, and some are not. Solutions of sugar and other neutral principles in water, are not affected by alcohol, unless in extreme proportions.

Alcohol ranks next to water as a solvent. It dissolves most organic bodies except the carbohydrates and protein bodies, such as alkaloids, glucosides, organic acids, neutral principles, volatile oils (only one fixed oil, viz.: castor oil), resins, balsams, camphors; and most of these are thrown out of solution by diluting with water. Many metallic salts are also soluble in alcohol. Prof. Frank X. Moerk has given the following statements regarding these:

"Metallic salts, soluble in alcohol and water, as a rule become more soluble as the alcohol is more dilute,—an exception is mercuric chloride.

"Metallic salts soluble in water are not necessarily soluble in alcohol. The converse, however, appears to be true with one important exception, namely: mercuric iodide, which, while soluble in alcohol, is not appreciably soluble in water.

"Metallic salts which *effloresce* are *not soluble* in alcohol. (Exceptions: lead acetate and sodium hydroxide.)

"Metallic salts which *deliquesce* are *soluble* in alcohol. (Exceptions: potassium carbonate and phosphate.)"

"The *metallic salts which are soluble in alcohol* are acetates (excepting mercurous, and silver), benzoates, bromides (generally), chlorates (excepting potassium chlorate), chlorides (excepting those of sodium, potassium, ammonium, silver, lead, and mercurous), iodides (excepting lead, silver, and mercurous), nitrates (excepting potassium, lead, and bismuth subnitrate), salicylates (excepting mercury and bismuth), and valerates."

"*Metallic salts insoluble in alcohol* are arsenates, arsenites, borates, bromates, carbonates, chromates, citrates, cyanides (excepting mer-

curic cyanide), ferricyanides, ferrocyanides, fluorides, gallates, hydroxides (excepting potassium, sodium and ammonium), hypochlorites, hypophosphites (excepting potassium, sodium and ammonium), hyposulphites (thiosulphates), nitrates, oxalates, oxides, permanganates, phosphates, pyrophosphates, silicates, succinates (excepting those of iron and the alkali metals), sulphates (excepting ferric and platinic), sulphides (excepting potassium, sodium and ammonium), tannates and tartrates."

It will be noticed from the above list that *most of the acetates, benzoates, nitrates, salicylates, valerates, and halogen salts (i. e., chlorides, bromides and iodides, which are mostly deliquescent) are soluble in alcohol, while nearly all others are insoluble, except those which are also deliquescent.*

Glycerin lies between alcohol and water in solvent properties, dissolving many bodies which are soluble in both. It is an excellent solvent for tannic acid, borax (which it decomposes, developing an acid reaction), phenol, gallic and boric acids, creosote, iodine, and many of the metallic salts. It also dissolves normal bismuth nitrate and other similar salts, which are decomposed by water. It has a striking property of dissolving most of the water-soluble metallic sulphates freely, all of which are insoluble in alcohol. Glycerin is unobjectionable therapeutically, and is therefore preferred to alcohol in many cases. It is frequently added to prescriptions in the place of a portion of the water, to hold bodies in solution.

Besides these solvents, the use of other salts to dissolve insoluble salts, as given in the table of compound solvents in the chapter on Mixtures, is sometimes allowable. This should be practiced very cautiously, as in some cases the medicinal action is altered thereby.

4. **Emulsifying, or suspending the troublesome body with gums or syrup.**—In cases where solution cannot be maintained or secured, it is often advisable to insure an even diffusion of the insoluble body by emulsifying it or incorporating it with a viscid liquid, so that it cannot settle quickly.

When acacia is used, it should be remembered that strong alcoholic liquids cannot be added directly, but a dilute mucilage must be made, to which the alcoholic fluid is gradually added.

Many resinous tinctures, fluid extracts, etc., are suspended in this way.

When tragacanth is used the best results are secured by adding the tincture or fluid extract directly to the powdered gum, and after shaking these together, water is added in the proportion of one of gum to twenty of water, and the mixture should be shaken vigorously until the gum is swollen. Insoluble salts are sometimes suspended by means of tragacanth. Syrup as a suspending agent is used mostly for bodies of light density.

CHEMICAL INCOMPATIBILITIES

Chemical incompatibility may be known in three ways: By precipitation, or the formation of insoluble compounds; by effervescence, or the evolution of gases; and by changes in color. The formation of a liquid from two solids is not necessarily an indication of chemical incompatibility, but will be included under this head.

Chemical incompatibilities are the most difficult of all to overcome, and in fact cannot be overcome except in very weak cases.

Glycerin and syrup will often retard changes, and in a few cases prevent it entirely. These are frequently used in cases where changes occur slowly, if at all.

When one of these is present it should be added to one of the suspected ingredients before adding the other. In the absence of these a good rule to follow is to *dilute the reacting ingredients to their full extent before mixing* (i. e., keep them as far apart as possible), and to mix them cold.

Precipitation, or the formation of insoluble compounds, forms the largest class of incompatibilities. These take place according to the general rule that *when two salts can by interchange of radicals form an insoluble salt in the liquid present, such insoluble salt will be formed and precipitated*. By the term salt is here meant all combinations of basic (positive) and acid (negative) radicals, acids being considered salts of hydrogen in this sense.

The salts which react may be both soluble, or one or both insoluble, since reactions can take place between dry and insoluble salts.

Insoluble salts are rarely inert, but they act more slowly upon the system than soluble salts. Thus we know that the antidote for poisoning by corrosive sublimate is white of an egg, an insoluble albuminate of mercury being formed, but if this insoluble albuminate is allowed to remain in the stomach the poisonous action will continue, though more slowly.

Consequently in cases of poisoning by metallic salts an antidote is first given, which, by reaction, will form an insoluble salt, then this is removed from the stomach by an emetic, the emetic being quite as important as the antidote.

Thus, because of the varying action of medicines in their different forms, incompatible mixtures may be purposely ordered. Whether this is the case in any particular mixture must be decided largely by the dispenser, since upon a proper interpretation of the physician's intentions depends the correct compounding of prescriptions. No positive rule can be laid down for determining this, except that a change in a mixture which results in compounds having a totally different therapeutic action from that of the original ingredients, cannot be considered as designed.

Furthermore, incompatibilities cannot always be foretold, and it may not be until after the prescription has been compounded that they are detected.

Each new prescription thus becomes "a law unto itself," and expertness in compounding is only acquired by combined study and experience.

In the following notes on solubility, etc., reference is made to *pure salts*, but it must be remembered that incompatibility is often due to impurities in the salts used.

Acetates are all soluble. Silver, mercurous and quinine acetates are sparingly soluble. Ferric and aluminum acetates become basic and insoluble, and many others lose acetic acid on exposure to the air, becoming carbonated.

With ferric salts, a deep red color is produced. Quinine is precipitated unless in strongly acid solution.

Acetic acid decomposes carbonates, but is itself displaced by the mineral acids.

Arsenates are mostly insoluble, except the alkali arsenates. These are apt to contain carbonate as an impurity and so have the incompatibilities of alkalis. In acid solutions arsenates act as mild oxidizing agents. They are reduced by hypophosphites and sulphites, and liberate iodine from iodides.

Arsenites are insoluble except those of the alkali metals. All are soluble in hydrochloric acid, and some in ammonium chloride or nitrate. The soluble arsenites act slowly as reducing agents. Ferric hydroxide and dialyzed iron precipitate arsenous acid and arsenites very completely. Many of the incompatibilities of arsenical solutions are due to acids or alkalis which they contain. Fowler's solution precipitates mercuric chloride and most of the metallic salts, also alkaloids, and tannin. Strychnine is precipitated as the arsenite. On exposure to air solutions of arsenites are partially oxidized to arsenates (Fowler's solution, etc.).

Benzoates are mostly soluble. They are easily decomposed by mineral acids, the benzoic acid being thrown out of solution. Silver, mercury, lead and quinine benzoates are sparingly soluble. Soluble benzoates precipitate neutral solutions of ferric salts as ferric benzoate, which is flesh-colored. Ferric benzoate is soluble in oils.

Benzoic acid is more soluble in solutions of sodium citrate or phosphate, and benzoates in sodium acetate than in water.

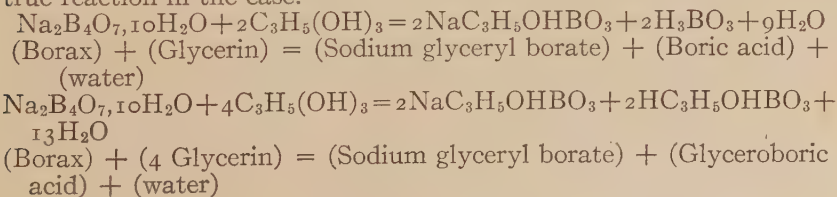
Borates are insoluble except those of the alkali metals, but the metallic borates are soluble in an excess of boric or tartaric acids, or in borax and tartrates.

Boric acid combines feebly with bases, and is easily displaced by mineral acids, or even by carbonic acid. It dissolves freshly precipitated zinc hydroxide.

Borax.—Borax is alkaline in reaction and precipitates salts of the metals, usually forming insoluble borates. With alum, aluminum hydroxide is precipitated. Borax precipitates alkaloids and gelatinizes mucilage of acacia in strong solutions, decomposes chloral, and dissolves benzoic, gallic, and salicylic acids.

Glycerin decomposes borax and changes its reaction from alkaline to acid, thus preventing the precipitation of alkaloids.

The reaction with glycerin is usually stated as forming first sodium metaborate and glyceryl borate, then the latter reacts with water to form boric acid and glycerol. This reaction is hardly in accord with chemical principles and does not satisfactorily explain the phenomena involved. Wm. Duncan, Ph. C., offers the following equations as the true reaction in the case.



That is, two molecules of glycerin to one of borax gives neutral sodium glyceroborate and free boric acid. Two molecules of glycerin are therefore necessary to change the reaction from alkaline to faintly acid. If, however, four molecules of glycerin to one of borax (which is about equal weights of the two) be used, then glyceroboric acid is formed, which is much more active chemically than boric acid, and decomposes carbonates vigorously. In the first reaction, an excess of water will gradually hydrolize the sodium glyceroborate and the reaction will again become alkaline. But in the second reaction the solution is permanently acid. Borax therefore requires about an equal weight of glycerin to prevent precipitation of alkaloids or metallic salts, or to cause effervescence with carbonates as in Dobell's solution. Glucose, honey, mannite and some other forms of sugars act similarly, hence Honey of Borax is acid in reaction. With mannitol borax combines in the proportion of one molecule with three molecules of mannitol.

With citric and tartaric acids, and with alkaline tartrates, borax forms very soluble compounds known as borocitrates or borotartrates. Similar compounds are formed with benzoic, gallic, salicylic and tannic acids.

Borax causes mucilage to become gelatinous, or may even precipitate the gum. This is overcome by sugar.

Bromides are soluble, except the mercurous lead, silver, bismuth, and antimony bromides, the latter two being decomposed by water. Organic bromine compounds are also decomposed by water. Mercurous bromide decomposes into mercuric bromide and metallic mercury, making calomel and other mercurous salts *dangerously incompatible* with bromides.

Oxidizing agents liberate free bromine. Soluble bromides precipitate some of the alkaloids as salts, particularly from strong solutions. This is prevented or reduced by syrup, glycerin or alcohol.

The alkali bromides sometimes contain traces of bromate (which liberates free bromine in contact with acids) and carbonate (which precipitates metallic salts as carbonates) as impurities.

Carbonates are insoluble, except those of the alkali metals. Most of the metallic carbonates are basic salts, and some of these are soluble in an excess of carbonic acid, bicarbonates being formed which are (many of them) soluble. Thus with very cold solutions bicarbonates can sometimes be mixed with certain metallic salts without precipitation, but in most cases an insoluble basic carbonate results, and an effervescence is caused by the escape of carbon dioxide. The carbonates are decomposed by all acids except hydrocyanic.

Chlorides are soluble, except those of lead, mercurous and silver. Hydrochloric acid is decomposed by strong nitric acid, nitrates and other oxidizing agents, liberating free chlorine.

Strong hydrochloric acid changes calomel, in part to corrosive sublimate, but weak acid changes it very slightly, if at all. Concentrated solutions of chlorides may precipitate alkaloidal salts. Hydrochloric acid gives reddish to brown colorations with resinous tinctures. (Ruddiman.)

Chlorates and Hypochlorites are all soluble. They are decomposed by strong acids (the former being fairly permanent if the acid

is very weak), liberating free chlorine. They also act as oxidizing agents in acid solutions. Their explosive properties are treated under "explosive mixtures." Sodium chlorate is much more soluble than potassium chlorate. Hypochlorites bleach vegetable colors. With strong hydrochloric acid, chlorates liberate chlorine and chlorine oxides.

Chromates are mostly insoluble in water, but soluble in nitric acid. They are powerful oxidizing agents, and the alkali chromates decompose many metallic salts, particularly in acid solutions. They must be mixed cautiously with alcohol, glycerin and other organic bodies. Fire or an explosion is liable to result from the incautious mixing of chromic acid or chromates with organic matter. The alkali chromates are soluble.

Citrates, except the alkali citrates, are mostly insoluble or sparingly soluble in water. Calcium citrate is more soluble in cold than in hot water. Citrate of magnesium crystallizes in three different forms, containing 3, 5, and 7 molecules, respectively, of water of crystallization. The first two are quite soluble in water, but the last is only sparingly so, and it is this salt which is said to deposit in solution of magnesium citrate bottles. The alkaline citrates (in neutral or alkaline solutions, but not in those which contain an excess of mineral acids) have the power of dissolving a large number of the insoluble metallic salts, notably those of iron, bismuth and lead. The scaled salts of phosphate and pyrophosphates of iron, and the elixir of phosphate of iron, etc., are instances of such. Soluble citrates prevent the precipitation of most metallic salts by alkalis, unless heated, and prevent the coloration of iron salts with tannin. The presence of an alkali citrate may prevent the precipitation of benzoic, salicylic or gallic acid, or may serve as a solvent of these acids and other organic bodies, such as acetylsalicylic acid. On the other hand strong solutions of citrates may cause the precipitation of quinine, strychnine, morphine, codeine, atropine and other alkaloids. Soluble bismuth citrate is precipitated by mineral, and by many organic acids. Quinine citrate is sparingly soluble and easily decomposed. The alkali citrates are insoluble in alcohol and are likely to cause the separation of alcohol.

Cyanides are insoluble, except those of the alkali metals, alkaline earths and mercuric. All are soluble, however, in an excess of potassium cyanide, or in hydrocyanic and other acids.

Hydrocyanic acid and potassium cyanide are decomposed in aqueous solution into formate and ammonia. Hydrocyanic acid combines feebly with bases, and is displaced even by carbonic acid. Calomel is changed to mercuric chloride and metallic mercury. Oxidizing agents decompose cyanides in strong solutions. When triturated with oxidizing agents in a dry condition, potassium cyanide is liable to explode.

The alkali cyanides usually have an alkaline reaction, and precipitate the alkaloids from their salt solutions.

Ferricyanides and Ferrocyanides are mostly insoluble, except those of the alkali metals and the alkaline earths. Most of them are soluble either in acids or caustic alkalis.

Ferricyanide of potassium acts as an oxidizing agent in alkaline solutions.

Ferrocyanides are easily decomposed by acids, liberating the poisonous hydrocyanic acid. (The ferri- and ferrocyanides are not,

in themselves, poisonous.) With weak acids the decomposition may be very slow. (Moerk.)

Glycerophosphates of the alkali metals are soluble in water and are likely to be alkaline. Glycerophosphates of alkaline earths are soluble in acid solutions, but are slowly decomposed by mineral acids. In solutions of citric, lactic and phosphoric acids the glycerophosphates are fairly stable. Alkalis decompose them, forming glycerin and phosphates. All of the glycerophosphates are easily precipitated by alcohol. Solutions are more stable when glycerin or syrup is present in considerable proportion. The glycerophosphates of the metals are sparingly soluble, iron and manganese glycerophosphate being soluble in alkali citrate solutions.

Gallates are mostly insoluble in water, with the exception of the alkali gallates. Many of the metallic gallates are soluble in alcohol and in acetic acid and in excess of gallic acid. Bismuth basic gallate is soluble in alkali solutions. Alkaloids are *not* precipitated by gallic acid, unless tannic acid is also present.

Gallic acid in aqueous solution turns black on exposure to air and decomposes. This is hastened by alkalis. Excess of alkali with gallic acid produces dark-colored solutions. With lime water, blue, green or pink colorations are produced. With ferric chloride the color is blue-black. Tartar emetic is precipitated by gallates. Also lead acetate. Gallic acid is decomposed by nitrous acid and other oxidizing agents. The solubility of gallic acid in water is increased by alkaline citrates.

Hydroxides are insoluble, except those of the alkalis and alkaline earths. They neutralize acids, forming the corresponding salts. The hydroxides of aluminum, zinc, lead, tin, gold, and platinum are soluble in excess of sodium or potassium hydroxide.

Alkaloids are precipitated by the fixed alkalies (hydroxides of sodium and potassium) and by ammonium hydroxide, some of them being also soluble in excess. Some alkaloids are decomposed by the fixed alkalis.

By exposure to air, hydroxides absorb carbon dioxide and are partially changed to carbonates. They decompose ammonium salts, liberating ammonia gas. Sugar, glycerin, and other organic bodies hinder or prevent the precipitation of metallic salts by hydroxides. Some organic bodies, as santonin, cantharidin, chrysarobin, emodin, resins, etc., are rendered soluble, and some, as chloral, glucosides, some alkaloids, salol, ethers, etc., are decomposed by alkalis. Fats and oils are saponified.

Hypochlorites are all soluble, but are very unstable, decomposing even in the cold. They are more permanent in alkaline solutions. Decomposition is hastened by sunlight and by heat. They are powerful oxidizing agents. They bleach vegetable colors.

Hypophosphites are mostly soluble in water, and are decomposed by most acids. They are strong reducing agents, changing under exposure to air or by contact with oxidizing agents to phosphates, which are mostly insoluble.

Mercuric chloride and calomel are reduced. Bismuth subnitrate is reduced and darkened. Trituration of hypophosphites with oxidizing agents must be avoided.

Hyposulphites, true, are seldom found. Sodium hypsulphite, so-called, is really sodium thiosulphate. This precipitates sulphur when in contact with acids. It is decomposed by boiling water.

It is also a strong reducing agent, and decolorizes solutions of iodine, forming sodium iodide and sodium tetrathionate. It also dissolves many of the insoluble salts of silver and mercury.

Iodides are all soluble except those of lead, mercury, silver and cuprous. All the iodides are decomposed by strong light, particularly in solution. Silver and lead iodide is soluble in strong solutions of potassium iodide but not in weak. Mercurous iodide is changed to mercuric iodide and mercury by soluble iodides, and mercuric iodide is dissolved by excess of potassium or sodium iodide.

The alkali iodides sometimes contain iodate, which liberates free iodine in contact with mineral acids. The soluble iodides are also decomposed by nitric and nitrous acids, and by ferric and cupric salts and other oxidizing agents, liberating free iodine.

Soluble iodides are more easily decomposed in acid than in alkaline or neutral solution. Calomel is changed into mercuric iodide and metallic mercury, by soluble iodides. Ferric chloride in acid solution, and spirit of nitrous ether liberate iodine.

Fowler's solution forms a precipitate with potassium iodide in strong solution. Alkaloids are precipitated by soluble iodides, particularly in strong solutions. A dark precipitate is slowly formed with creosote.

The alkali iodides are excellent solvents for iodine and for insoluble iodides. Many iodides are soluble in alcohol.

Iodine in alkaline alcoholic liquids forms iodoform, hence tincture of iodine is incompatible with the weakest alkalis. An excess of alkali forms the colorless iodide. It also forms colorless compounds with fixed and volatile oils, tannin, some sugars, some organic bodies, hydrocyanic acid, hypsulphites, sulphites, and alkaline carbonates, and hydroxides.

Iodine decomposes methyl alcohol in part, forming formic acid and formaldehyde, which are very irritating. With ammonia water an explosive compound may be formed. Oxidizing agents change iodine to iodic acid, and reducing agents form colorless iodides or hydriodic acid. With starch a blue compound is formed.

Iodine acts as an oxidizing agent, and changes mercurous to mercuric salts. Most alkaloids are precipitated by iodine solutions.

Lactates of the alkali metals are soluble, those of the alkaline earths are sparingly soluble. The others are insoluble, except in alkaline lactate or citrate solutions.

Nitrates are all soluble. Bismuth nitrate is soluble in glycerin, but is decomposed by water, forming the basic "subnitrate." Nitric acid is a powerful oxidizing agent, and is reduced, sometimes with explosive violence, by organic matter. It also decomposes chlorides, bromides, and iodides unless diluted.

Strong nitric acid should not be mixed with organic matter (alcoholic tinctures, etc., oils, or dry organic compounds) but weak nitric acid may often be combined with organic bodies. With salicylic acid the reddish nitro-salicylic acid is formed. Strong nitric acid gives color reactions with many of the alkaloids and with aloe, phenols, etc.

With glycerin the explosive nitroglycerin may be formed. This does not form in the presence of a considerable proportion of water.

Nitrites are soluble, but silver and lead nitrites are only slightly soluble. As a rule nitrites are less soluble than the nitrates. Neutral nitrites are generally compatible, but in acid mixtures nitrous acid is liberated, which acts sometimes as an oxidizing and sometimes as a reducing agent. Spirit of nitrous ether is troublesome for this reason, decomposing easily and liberating free nitrous acid, which then reacts with liquids containing tannin (liberating nitrous fumes), with iodides (liberating iodine), etc. With tannic acid nitrous oxide is liberated. These reactions may be prevented, or at least hindered, by first neutralizing the spirit of nitrous ether with potassium bicarbonate.

Nitrous acid reduces mercury salts, both mercuric and mercurous, permanganates, chromates and some of the metallic salts.

Antipyrin gives a green solution, acetanilid a yellow, sodium salicylate a reddish brown, phenol a brown, thymol a brown, guaiac a blue color with nitrous acid and nitrites.

Oxalates are mostly insoluble. Tetroxalate of potassium dissolves several of the insoluble salts of iron, tannate, etc.

Oxides are all insoluble except the alkali oxides which form hydroxides with water. The only oxides from which trouble is to be anticipated in prescriptions are chromic and silver oxides and the peroxides. All these are oxidizing agents, and should be prescribed alone.

Permanganates are all soluble. They are strong and sensitive oxidizing agents, and should not be mixed with organic bodies, reducing or oxidizing agents. Pills of permanganates are made with kaolin and a fatty excipient.

Peroxides.—Sodium peroxide is decomposed by water rapidly, forming sodium hydroxide and liberating oxygen. The peroxides of calcium, magnesium, strontium and zinc are practically insoluble in water but are slowly decomposed in its presence, liberating oxygen. Acids decompose these rapidly, forming hydrogen peroxide which liberates oxygen slowly or rapidly according to conditions and the presence of oxidizable substances. The peroxides are all incompatible with organic matter, and with reducing agents. (See Hydrogen Peroxide.)

Phosphates, except the alkali phosphates, are nearly all insoluble, but are soluble in excess of phosphoric, nitric or hydrochloric acid. Some are also soluble in solutions of organic acids, under favorable circumstances. The insoluble phosphates are also soluble in alkali citrates, except magnesium phosphate, and these are miscible with metaphosphoric acid.

Ferric chloride is decolorized by phosphoric acid, and the solution is not blackened by tannin. Soluble ferric phosphate is precipitated by phosphoric acid, the precipitate being soluble in excess. Metaphosphoric acid does not cause a precipitate with soluble phosphate or pyrophosphate of iron.

Salicylates.—Salicylic acid and quinine salicylate are the most important of the *insoluble* salicylates met with in pharmacy. Sodium salicylate is slightly acid in reaction, since if alkaline it is discolored.

Solutions of salicylates turn brown on exposure to air, particularly if alkaline. Sodium bicarbonate or carbonate causes the darkening

to appear more rapidly and more deeply than hydroxide. The darkening is probably due to oxidation in an alkaline medium, since it is hindered or even prevented by the addition of reducing agents, such as sodium bisulphite, thiosulphate, etc.

A strong solution of sodium salicylate dissolves volatile oils, resins, creosote, phenols, menthol, etc. Salicylates give a violet to red color with ferric chloride, a green with copper salts, a red or brown with bismuth subnitrate and free nitric or nitrous acid. Salicylic acid liberates iodine slowly from potassium iodide, and sodium salicylate slowly combines with free iodine. The free acid is rendered more soluble in water by the presence of soluble citrates, phosphates, etc. Salicylates appear to intensify the action of mercurials, sometimes causing salivation when combined with calomel.

Salicylate of sodium forms a damp mixture when triturated with exalgin, urethane, lead acetate or sodium phosphate (Ruddiman). Mineral acids liberate salicylic acid from combination.

Succinates are mostly soluble. The insoluble succinates are dissolved by potassium acetate or citrate solutions.

Sulphates are soluble in water, except those of barium, strontium, calcium, lead, antimony, and mercurous. Most of the water soluble sulphates are soluble in glycerin, but nearly all are insoluble, or but slightly soluble in alcohol. Concentrated sulphuric acid chars most organic bodies. Dilute acid does not.

Sulphides are insoluble, except those of the alkali metals and alkaline earths. All are decomposed easily by acids.

Sulphites are mostly insoluble, except those of the alkali metals, but soluble in acetic and mineral acids. They are oxidized to sulphates by air and oxidizing agents. Acid solutions of sulphites bleach vegetable colors. They reduce mercury salts and other metallic salts, as well as oxidizing agents.

Tannates are very unstable, and the basic salts of the heavier metals are insoluble, hence the metallic salts in general yield precipitates when in contact with preparations containing tannin. Gelatin, starch and albumin are also precipitated by tannin. Potassium, ammonium and calcium hydroxides, and potassium carbonate, not in excess, precipitate tannic acid from solution. The precipitate is soluble in excess of alkali and becomes dark colored. Very soluble neutral salts may throw tannin out of solution. Aqueous solutions of gallotannin slowly decompose into gallic and ellagic acids. The solution forms hydriodic acid with iodine. Tannin acts as a reducing agent on salts of mercury, silver and copper and should not be triturated with dry oxidizing agents. In solution, the tannin is decomposed by oxidizing agents. Tannic acid precipitates tartar emetic, arsenites and arsenates, some glucosides and most alkaloids, the latter being soluble in alcohol. Colored compounds are formed with iron salts and other metallic salts.

Tartrates.—The normal tartrates are mostly insoluble, but the acid tartrates are mostly soluble, potassium and ammonium bitartrates being notable exceptions.

Rochelle salt with most acids forms potassium bitartrate, which deposits. Soluble tartrates with potassium salts form potassium bitartrate unless the solution is alkaline. The formation of potassium

bitartrate is prevented by boric acid and borax. Tartaric acid is a weak reducing agent, and reduces salts of silver, gold and mercury under favorable conditions. Soluble tartrates prevent precipitation of metallic salts in very many cases. Tartar emetic is precipitated by alcohol and by tannin.

Valerates are mostly soluble, but are decomposed by many acids, liberating insoluble valeric acid. In mixtures, elixirs, pill masses, etc., the objectionable odor and taste of valerates is covered by the presence of a slight excess of ammonia or other alkali.

Acids form salts with alkalis and alkaloids, and cause effervescence with carbonates.

The mineral acids displace the weaker organic acids from their salts, and these may be thrown out of solution. They also dissolve oxides.

They precipitate bismuth citrate from solutions of bismuth and ammonium citrate, and tartrate from solution of bismuth and sodium tartrate.

It should be borne in mind that acids are contained in the official vinegars (aceta), in fluidextracts of ipecac, ergot, and sanguinaria, tincture of sanguinaria, syrups of citric acid, hydriodic acid, orange, garlic, calcium lactophosphate, hypophosphites, ipecac, lemon, and squill, in citrate of iron and quinine, solution of acetate of iron, of arsenous acid, of ammonium acetate, of chlorine, of ferric chloride, of ferric nitrate, and infusions of cinchona and rose, paregoric, Basham's mixture, hydrogen peroxide solution, oleates of mercury and veratrine.

Besides these some articles become acid on exposure, as acetic ether, nitrous ether, etc., and most galenical preparations are slightly acid.

Alkalis are incompatible with acids, with metallic salts, alkaloid salts, chloral, and, in strong solution, with organic matter in general. Some organic bodies, as santonin, cantharidin, chrysarobin, emodin, resins, etc., are rendered soluble in water by alkalis, and some, as chloral, glucosides, some alkaloids, salol, ethers, etc., are decomposed. Fats and oils are saponified.

A large number of pharmaceutical preparations contain alkali, particularly those of rhubarb, senega, eriodictyon and pancreatin, and some of catnep, guaiac, licorice, and asarum, also some liniments, lotions, elixirs and mixtures.

Aluminum.—The borate, hydrate, oxalate and phosphate are insoluble. Citrates, tartrates, glycerin and sugar tend to prevent precipitation. Alum and aluminum sulphate precipitate organic and coloring matters from impure water, and are sometimes used for this purpose when a clear and colorless water is desired in large quantities for washing white precipitates, etc. Alum is precipitated by alkalis unless prevented by glycerin or syrup.

Dried alum is very slowly soluble, and may be partially insoluble if overheated in drying.

Alum is soluble in both water and glycerin, but the addition of glycerin to a strong aqueous solution, or the dilution with water of a glycerin solution has caused crystallization.

Ammonium.—The bitartrate is only slowly soluble. All the ammonium salts are decomposed by potassium and sodium hydroxides and carbonates, liberating gaseous ammonia.

Ammonium acetate, bromide, iodide and valerate are very unstable, losing both ammonia and acid. For this reason the first is known to pharmacists only in solution. Ammonium carbonate loses both carbonic acid gas and ammonia, and leaves bicarbonate. Ammonium carbonate and hydroxide form double salts with mercuric chloride, and a black compound with calomel. They are not as active precipitants as the fixed alkali hydroxides and carbonates.

Ammonium hydroxide is official in three forms, as water of ammonia, stronger water of ammonia and anisated spirit of ammonia. The spirit of ammonia is intended for use in mixtures in which water would cause precipitation, the former alcoholic solution being clearly miscible with collodion, tinctures, etc. Care should be used in mixing ammonia water and spirit with preparations containing free iodine or chlorine lest the highly explosive compound NHI_2 or the chlorine compound be formed.

Ammonium chloride tablets containing potassium chlorate have also been known to explode.

Ammonium salts, particularly the acetate, citrate and chloride, have the property of dissolving many of the insoluble salts of the heavy metals.

Antimony.—Only the acetate and tartrate are soluble, but many of the other salts are soluble in strongly acid solutions. Solutions of the tartrate are liable to decompose slowly unless free acid is present. Tartar emetic is precipitated by nitric, hydrochloric and sulphuric acids, by tannin, alcohol and alkalis. Antimony chloride is reduced in aqueous solutions.

Antimony salts precipitate tannin, mucilage and albumin.

The sulphides and oxide are used only in powders, and the former should be mixed cautiously with oxidizing agents.

Tartar emetic (antimony and potassium tartrate) is found in tincture of antimony, in compound syrup of squill, and in Brown Mixture.

Arsenic.—Arsenic and its compounds act as acids in most cases. The sulphide is insoluble in acid, but soluble in alkaline solutions. The oxide is not easily compatible with other bodies in fluid form, and is used largely in pills, where, owing to its very slow and slight solubility, reactions do not occur easily. There are five solutions official, all but one of about the same strength and dose, and intended chiefly to be chosen in regard to compatibility. One is an acid solution, one an alkaline, and three are neutral.

Solution of arsenous acid, "Valangin's Solution," is acid with hydrochloric acid, and is intended for admixture with tincture of chloride of iron and similar preparations. Solution of potassium arsenite, "Fowler's Solution," is alkaline with potassium carbonate, and is intended for use in neutral or alkaline mixtures in the absence of metallic salts. Fowler's solution is partially oxidized to arsenate on standing, but this change is not of importance in dispensing. Solution of sodium arsenate and the Diluted Solution are neutral and also contain the arsenic in an *ic* condition, so that they are more compatible with oxidizing agents. Solution of arsenic and mercury iodides, "Donovan's Solution," is also neutral. It is precipitated by alkalis, and is itself precipitant of alkaloids and silver salts, hence it

is incompatible with solutions containing alkaloids, unless sufficient alcohol be present to hold these in solution.

There are several organic compounds of arsenic in use which are less toxic than the mineral solutions and salts, and are sometimes preferred on account of a slower or a more specific action. They are fairly stable compounds, mostly soluble in water but insoluble or slightly soluble in alcohol, and causing little trouble by incompatibility. They include:

Arrhenal (sodium methyl arsenite), readily soluble in water but incompatible with mercuric chloride and with alkaloids.

Arsphenamine or **Salvarsan** and **Neoarsphenamine** (diaminodioxo-arsenobenzene), the former an acid and slightly soluble and the latter a neutral and soluble form, are easily and rapidly oxidized. These are mostly given alone. Neo-salvarsan decomposes rapidly on exposure to air, and the sealed tubes containing it should not be opened until immediately before use.

Atoxyl (sodium aminophenyl arsenate).

Sodium Cacodylate very soluble in water and has a slightly alkaline reaction.

Barium.—The carbonate, chromate, cyanide, oxalate, peroxide, phosphate, sulphate, and sulphite are insoluble. Barium salts are very poisonous and are never used internally, except the insoluble barium sulphate which is used for x-ray diagnosis. This must not be confused with the sulphide.

Bismuth.—Only the acetate is soluble. The nitrate is soluble in a moderately strong solution of nitric acid, but on dilution a basic oxynitrate is precipitated. Similarly the chloride is soluble in hydrochloric acid but is precipitated on dilution with water. These acid solutions are not suitable for internal use, being too strongly acid, hence the solutions of bismuth salts which are employed internally are double salt solutions. Organic acids, as citric, tartaric, salicylic, gallic acids, etc., form compounds which are soluble in the corresponding alkali salts, or in alkaline solutions. Double salts are thus formed, as the ammonio-citrate and the sodio-tartrate which are soluble in water. These solutions are easily decomposed by acids, when the normal citrate or tartrate of bismuth separates out. The ammonio-citrate is particularly sensitive and its solution must be faintly alkaline to be stable. The sodio-tartrate is less sensitive and can be held in solution in faintly acid liquids.

Bismuth nitrate (not the subnitrate) is slowly soluble in glycerin, but should not be triturated therewith lest an explosive decomposition be induced. Bismuth subnitrate when suspended in water is slowly hydrolyzed, liberating nitric acid and forming a more basic bismuth oxynitrate. The liberated acid will then effervesce with carbonates and bicarbonates, liberate salicylic acid from salicylates, iodine from iodides, and respond to the usual incompatibilities of nitric acid. Hence bismuth subcarbonate is more suitable for liquid mixtures in which the bismuth is combined with carbonates or other reactive salts.

Bismuth subnitrate is reduced and blackened by hypophosphites, formaldehyde and other reducing agents. It is also reduced by invert

sugar in alkaline solution. This occurs very slowly on standing but rapidly if heated. When bromides are present the liquid may be photosensitive, *i. e.*, may form a black mirror on the bottle when in the light and this may be redissolved and the liquid lightened or even whitened in color by storing in the dark. Bromides without sugar cause a slow darkening in the light.

Bismuth salts if alkaline form a yellow solution with soluble iodides. If the liquid is acid the red oxyiodide is precipitated, which changes to black on standing. With salicylates, bismuth subnitrate forms the red nitro-salicylate.

Most of these reactions are slow, often requiring several hours before they become noticeable, hence they must be foreseen in prescriptions.

Dr. H. A. B. Dunning finds that the compact form of bismuth subnitrate hydrolyzes and becomes strongly acid in water more rapidly than the more bulky kinds, and that heat promotes the reaction. The reaction is slower in aromatic waters, as peppermint water, than in pure water, and is also retarded by alcohol, glycerin, and syrup. Sodium bromide accelerates it. Mixtures of the subnitrate with aqueous fluids in time become very strongly acid and unpleasant to take. Glycerin or syrup are better aids to suspension than gums or starch.

The solutions of bismuth in use are those of the ammonio-citrate, in which bismuth citrate is dissolved in a solution of ammonium citrate, and the bismuth and sodium tartrate solution and glycerite of the N. F. Acids decompose both salts, and precipitate the bismuth as a normal citrate, or tartrate.

Bismuth subgallate is soluble only in alkaline solutions, is decomposed by mineral acids, and is used mostly in powder form or suspension. It is a type of a number of compounds (bismuth subsalicylate being another) of similar character, insoluble in water or ordinary solvents and decomposed by hot water or mineral acids, such as

Airol,—bismuth oxyiodosubgallate,

Bismal,—bismuth methylene digallate,

Bismutose,—bismuth biproteinat

Dermatol,—bismuth subgallate,

Dermol,—bismuth chrysophanate

Helcosal,—bismuth pyrogallate, etc.

Airol slowly liberates iodine in presence of moisture.

Calcium.—The arsenite, borate, carbonate, citrate, fluoride, oxalate, phosphate, sulphate, and tartrate are insoluble. Calcium hydroxide and citrate and glycerophosphate are more soluble in cold than in warm water, and the hydroxide is much more soluble in syrup than in water. On the other hand, calcium hypophosphite is thrown out of solution by an excess of sugar. The carbonate is soluble in water charged with carbonic acid gas, becoming bicarbonate.

Copper.—Only the acetate, chlorate, chloride, nitrate, permanganate and sulphate are soluble, the other salts insoluble. Ammonia water dissolves the hydroxide, producing an intensely blue solution and this solution dissolves filter paper, cotton, etc. (Much depends upon the condition of the ammonio-copper solution as a solvent for cellulose; it oftentimes fails to act well for this purpose.) Arsenites

precipitate green arsenite of copper. Soluble iodides precipitate cuprous iodide, and liberate iodine. Tannic acid precipitates, and may reduce, copper salts. In alkaline solutions copper salts are reduced to oxide by glucose and other reducing sugars.

Gold.—Only the bromide and chloride are soluble. Gold salts are reduced with extreme ease by all reducing agents, including ferrous salts, etc., the gold being deposited as a brick-red powder. Alkaloidal salts form insoluble double salts. Potassium iodide precipitates aurous iodide and liberates iodine.

Iron.—Reduced iron frequently contains some sulphide which may be troublesome if used for manufacturing small quantities of a salt by dissolving the iron in an acid or in making ferrous iodide. Sulphuretted hydrogen is thus formed, a part of which will remain in the liquid.

Ferrous arsenate, arsenite, borate, carbonate, cyanide, ferricyanide, hydroxide, oxalate, phosphate, sulphide, tannate, and tartrate are insoluble. The pure ferrous salts are all bright green or white, but they oxidize readily and darken in color, becoming bluish or reddish-brown. They should be preserved in the light and in well-stoppered bottles. Sunlight will sometimes restore a solution which has partially oxidized. Sugar, acids, soluble chlorides, and glycerin hinder the oxidation. They are all incompatible with oxidizing agents.

The alkali citrates dissolve the insoluble ferrous salts and also modify their astringent taste.

Ferric arsenite, borate, chromate, carbonate, ferrocyanide, hydroxide, oxalate, phosphate, sulphide and tannate are insoluble. Ferric salts are reddish-brown in color (except the true phosphate), and should be preserved from the light, which reduces them. The double citrates and tartrates are red or olive green in color.

Those containing a volatile acid radical, as the acetate, chloride, nitrate, etc., easily lose a portion of the acid and become basic and insoluble. These may be restored by the cautious addition of a little acid, with the aid of a gentle heat, except the acetate, nitrate, and subsulphate, the last of which should be rejected or turned into tersulphate when it refuses to dissolve by aid of heat.

Alkali citrates, chlorides and sugar dissolve many of the insoluble salts of iron. This is the case with most of the scale salts, which are combinations of a salt of iron with an alkali citrate or tartrate. Tincture of ferric citrochloride is of the same strength in iron as tincture of ferric chloride, but the former avoids many of the incompatibilities of the latter because of the presence of sodium citrate.

The iron is not precipitated from these by addition of an alkali, except on heating, but small amounts of mineral acids will sometimes decompose them by destroying the alkali citrate or tartrate. An excess of the same mineral acid will usually re-dissolve the iron salt.

Ferric salts in solutions containing free citric, tartaric, lactic, or succinic acids, are reduced by light and **decompose the acids**, liberating carbon dioxide and causing pressure.

This action is slow, and has often been erroneously attributed to fermentation. The pressure generated is sufficient to burst the bottle after a few hours. The action does not occur in neutral or alkaline solutions, nor in absence of light. Ferrous salts do not react in this way.

Iron hydroxide and oxide is dissolved by sugar, under proper conditions (*i. e.*, when the hydroxide or oxide is free from excess of alkali), and this solution does not show the common reactions of iron unless acidulated. Dialyzed iron acts in the same way as the hydroxide, and may be used as a (poor) substitute for the latter in arsenical poisoning.

Dialyzed iron is rendered more stable by the addition of glycerin. This often prevents precipitation.

The inorganic ferric salts liberate iodine from potassium iodide. Ferric acetate does not do this, but will decompose syrup of hydriodic acid, liberating free iodine. This is one reason for the use of syrup and pills of ferrous iodide, the former of which is compatible with the soluble iodides.

Ferric chloride is incompatible with silver and mercurous salts, with alkalis, arsenites and arsenates, borax, albumin, casein, vegetable extracts and infusions; it gelatinizes mucilage of acacia, and gives colored compounds with many organic bodies, particularly those containing tannin. (See page 440.)

Lead.—The acetate, subacetate, chlorate, nitrate and nitrite are soluble; all other salts insoluble. Solution of subacetate of lead carbonates on exposure to air, or on diluting with water which has stood contact with air and dissolved carbonic acid gas. The subacetate is alkaline in reaction, and precipitates most vegetable coloring matters, most organic acids, and acacia. In many cases, glucosides and alkaloids are precipitated also. It emulsifies with oils and fats, making smooth liniments or ointments.

Lead sulphate is sometimes desired as an astringent in lotions, and is formed by reaction between a soluble lead salt and a soluble sulphate, in preference to using the dry and less diffusible salt.

Lithium.—Most of the lithium salts are soluble, the carbonate and phosphate being least so. Soluble carbonates and phosphates precipitate lithium carbonate or phosphate from strong solutions. The carbonate is quite soluble in water containing carbonic acid gas.

Magnesium.—The arsenate, borate, carbonate, hydroxide, oxalate and phosphate are insoluble.

The carbonate is quite soluble in carbonic acid water, and soluble magnesium salts may be mixed, under favorable conditions, with solutions of alkali bicarbonates (not carbonates) without precipitation. The official magnesium carbonate always contains some hydroxide, which is slightly soluble, and gives an alkaline liquid. The light oxide of magnesia hydrates and absorbs fifteen times its weight of water, forming a gelatinous mass. Also with sixteen times its weight of copaiba. This property of absorbing water often makes trouble when magnesium oxide is directed in mixtures, because it may form a mass which is too thick to pour, or even too hard to break up. Upon standing it may set to a cement-like hardness. It must also be used cautiously in pill masses lest the pills get so hard as to be insoluble.

Manganese.—The borate, carbonate, hydroxide, oxalate, oxide, phosphide, sulphite and sulphide are insoluble in water.

Manganese salts resemble iron salts in general properties being more soluble in sodium citrate solutions than in water. Except the glycerophosphate, citrate, hypophosphite and (less frequently) the sulphate, they are rarely used.

Mercury.—All the *mercurous* salts are insoluble in water, except the nitrate, and this is decomposed on diluting largely, a basic salt being formed.

The **mercurous salts**, except the chloride, are easily reduced by heavy trituration, contact with metals or reducing agents, and by mixing with certain salts. In all these cases metallic mercury and a mercuric salt are formed.

Hence, mercury salts in general, and mercurous salts in particular, should not be triturated heavily when dry. If necessary to pulverize them (except mercurous chloride) they should be moistened with a little alcohol, water or oil, before rubbing in a mortar.

Sunlight decomposes all mercurous salts, usually turning them dark. Some alkaloids also reduce and blacken calomel and other mercurous salts. Calomel is very sensitive to metals and reducing agents in the presence of moisture.

The most common and important incompatibilities of calomel and yellow mercurous iodide are soluble cyanides (rare), bromides and iodides. These change the mercurous salts to mercuric, and metallic mercury separates. The mercuric salts are so much more toxic than the mercurous that a poisonous dose is quite likely to result. The change is usually shown by the color as the mercury separates in a finely divided condition. Fowler's solution acts in the same way—producing mercuric chloride from calomel. Organic compounds of iodine, such as iodoform, thymol iodide, etc., have the same action. These combinations are dangerous and must be avoided.

Chlorides do not act easily upon calomel. Strong hydrochloric acid will change it to mercuric chloride, but weak acid has so little effect that it may be ignored. Sodium chloride is said to produce a trace of mercuric chloride from calomel, but this combination is not very uncommon, and is considered safe.

Thorough diffusion of calomel through a powdered diluent improves its action. This is the reason for calomel triturates, by which small doses of calomel are made effective.

Contact with alkalis changes mercurous salts to the black mercurous oxide.

Both oxidizing and reducing agents form mercuric compounds from the mercurous. The oxidizing agents change it completely when acid is present, and the reducing agents act to form mercury and the mercuric salt. Iodine, potassium chlorate, sodium nitrite, spirit of ethyl nitrite, hypophosphorous acid, and sulphites are the most probable combinations of this sort to be encountered.

Most of the mercurous salts are liable to contain traces of the corresponding mercuric salts as impurities.

Mercuric albuminate, arsenate, arsenite, carbonate, ferrocyanide, iodide, iodate, oxalate, oxide, phosphate, sulphide and tartrate, are insoluble. Alkalis, except ammonia, precipitate the yellow oxide.

Except the chloride, all the soluble salts require the presence of free acid for complete solution, being decomposed by water.

Soluble carbonates and borax precipitate basic salts. Borax forms the brick-red oxychloride. (Borax is contained in ointment of rose water.)

The mercuric chloride is more soluble and stable in solution of ammonium chloride; mercuric iodide is readily soluble in solution of potassium or sodium iodide, and slightly soluble in fixed oils.

The double salt formed by mixing solutions of mercuric chloride and potassium iodide, which is known as Mayer's solution, precipitates all alkaloids from acidulated aqueous solutions, except caffeine, colchicine and theobromine, but these precipitates are soluble in alcohol. Similar double compounds are formed with alkali chlorides and bromides.

In a few cases, concentrated solutions of mercuric chloride precipitate alkaloids, and, rarely, some other proximate principles, precipitation depending upon the strength of the solutions.

Mercuric salts also precipitate albumin, gelatin and tannin, the first (albumin) being given as an antidote to corrosive sublimate poisoning. It is well to know, however, that mercuric albuminate is soluble in excess of albumin and in ammonium chloride solution, and the white of one egg may therefore be better as an antidote than the whites of half a dozen. A prompt emetic is necessary in all cases.

Precipitation of mercuric salts is hindered or prevented by soluble chlorides, bromides, iodides, citrates, tartrates, glycerin, sugar or acacia.

Ammoniated mercury is slowly decomposed by water. It is quickly attacked by iodine, and may form the explosive nitrogen-hydrogen-iodide.

Mercuric salts are reduced by most reducing agents, including metals, arsenites, tartar emetic, ferrous salts, alcohol, honey, etc.

Potassium and Sodium.—Only potassium bitartrate is insoluble of the common salts.

Trouble with these is more likely to be found in the impurities than in the salts themselves. Thus the iodides sometimes contain small quantities of iodate, which is decomposed by acids, liberating free iodine. The iodate is also poisonous.

When iodides are mixed with spirit of nitrous ether, the latter should be neutralized before mixing, since the presence of mere traces of nitrous acid will liberate the iodine. Such mixtures cannot be kept long without change, unless the nitrous ether is entirely decomposed.

The hypophosphites frequently contain excess of sulphates, which are troublesome when mixed with calcium hypophosphite.

The bicarbonates are readily reduced to carbonates by heat or by hot water.

Carbon dioxide is liberated from solutions of potassium and sodium bicarbonate or carbonate by bismuth subnitrate or subsalicylate, lead acetate, zinc salts, magnesium salts, and slightly by lithium benzoate. Acetylsalicylic acid liberates the gas slowly but when sufficient is present, completely.

Silver.—The acetate, chlorate, lactate, nitrate, nitrite, hypophosphite and sulphate are soluble.

All of the silver salts are reduced by light, by organic matter and by reducing agents. They blacken as they become reduced by these agents. They should not be allowed to come into contact with metals (steel spatulas) or with vegetable matter. Solutions should be dis-

pensed in bottles of amber glass to protect them from reduction by light. The oxide is quite unstable and is liable to explode if triturated with organic matter or with ammonia salts.

Silver chloride is soluble in ammonia water and in hypophosphite and hyposulphite solutions. Silver iodide is soluble in a strong solution of potassium or sodium iodide, but is precipitated on dilution with water. Silver nitrate reacts quickly with all organic matter and precipitates albumin, the latter quality limiting its use as an antiseptic.

Colloidal solutions of silver or silver compounds are commonly used as antiseptics because they do not precipitate albumin and are thus more penetrating. There are a number of these in use, and their solutions react very slowly with chlorides, bromides and iodides so that such combinations may be dispensed. These compounds do not form permanent solutions, but with most of them solutions are obtained which are suitable for use for two or three days.

They are mostly colloidal or semicolloidal solutions of silver or silver oxide protected by gelatin, casein, nuclein or some other form of protein. Some are labelled as silver "proteinate," "caseinate," "nucleate," etc. They vary in the amount of silver which they contain, from 5 per cent to 75 per cent. Their activity as antiseptics does not depend upon the amount of silver contained in them, but upon its condition, and the latter is not yet thoroughly understood.

The commercial preparation which contains 50 per cent or more of silver, is **Collargol**.

The larger number contain less than 25 per cent of silver, and the Pharmacopœia divides them into two classes, Mild Silver-protein, containing 19 to 25 per cent of silver, and Strong Silver-protein, containing 7.5 to 8.5 per cent of silver. The terms "mild" and "strong" here refer to the activity rather than to the silver-content.

To the "mild" class belong **Argol**, **Argyrol**, **Cargentos**, **Neosilvol**, **Silver Nucleinate** (certain brands) **Silvol**, **Solargentum**, **Sophol**, etc.

To the "strong" class belong **Protargol**, **Silver Proteinate**, **Silver Nucleinate** (other brands,) **Hegonin**, etc.

Besides these there are some which do not come strictly within the Pharmacopœial specifications, such as **Albargin** (15 per cent) **Argonin** (5 per cent), **Nargol** (10 per cent) **Novargan**, etc.

These are all insoluble in and precipitated by alcohol, but are soluble in water. Most of them give very dark solutions but a few are light in color. They are likely to gum together if water is poured upon them, then dissolve very slowly, but solutions can be made quickly if they are sprinkled upon the water and immediately shaken for a minute or two. Solution is also aided by wetting them first with glycerin, then adding the water and agitating quickly. They precipitate slowly with neutral chlorides, more quickly with acids or acid salts, and some are immediately precipitated by tannin solutions. All of them are best dispensed without admixture of other antiseptics or remedies. When used in ointment or paste form they should be dissolved in water before incorporating with the base. Some are slightly alkaline in reaction, which adds to their potential incompatibilities.

Strontium salts are almost identical with the calcium salts in their chemical properties.

Tin salts are little used except as reagents.

Zinc.—The arsenate, borate, carbonate, cyanide, hydrate, oxalate, oxide, phosphate, sulphide and tartrate are insoluble. Zinc salts are used externally as mild astringents, but are seldom used internally. The oxide is liable to be gritty, preventing the formation of a smooth ointment. Only the fine pharmaceutical grade should be used.

Zinc chloride is hydrolysed by water (more than 5 parts) forming zinc oxychloride and hydrochloric acid. For eye lotions, boric acid in quantity equal to the zinc chloride should be added, or one fifth the weight of ammonium chloride should be mixed with the zinc chloride to obtain a permanent solution. Without these the solution may become cloudy and be irritating.

ORGANIC BODIES.—**Alkaloids** are vegetable alkalis and usually are the active constituents of the plants from which they are derived. They are mostly powerful medicinal agents, many of them being potent poisons. They combine with acids to form salts, in which form they are mostly used. No other plant-principles do this, and consequently alkaloids may be known by their existence in commerce as sulphate, hydrochloride, hydrobromide, acetate, etc. In the plants they are combined with organic acids peculiar to the plants, as igasuric acid in *nux vomica*, meconic acid in opium, quinic acid in *cinchona*, etc. It is important to remember this, since these organic acids oftentimes form insoluble salts with metallic bases, and salts of the heavier metals are therefore incompatible with many preparations of alkaloidal drugs (tinctures, fluid extracts, etc.). In many cases the alkaloid is carried down with the metallic precipitate.

The incompatibilities of alkaloids are numerous, and perhaps, the most important of any class of bodies because of their potency and the liability of an overdose being taken at the last when the bottle is not shaken each time.

Fortunately, nearly all the *incompatibilities of alkaloids can be overcome by glycerin or syrup, or by alcohol*, a strength of 15 to 40 per cent of alcohol sufficing in most cases. Thus, the incompatibilities of alkaloidal tinctures, fluid extracts, etc., may, for the most part, be disregarded, when a considerable proportion of alcohol is present in the mixture.

When alcohol is not permissible glycerin, syrup or mucilage should be employed. If these do not prevent precipitation they at least aid in holding the precipitate in suspension. Many of the alkaloidal precipitates are sticky and adhere to the sides of the bottle, or collect in masses unless means are taken to prevent. About a drachm to a drachm and a half of mucilage of acacia per ounce of mixture may prevent this, and produce a safer as well as a more elegant preparation.

Sometimes the alkaloidal salts are thrown out of solution as such by other salts. Thus strychnine salts are mostly insoluble in strong solutions of inorganic salts, but the addition of alcohol to the extent of 12 per cent of the mixture holds them in solution.

The principal precipitants of alkaloids are:

Alkalies and Borax.—These decompose the salts of the alkaloids, liberating the latter as free bodies, which are insoluble in water (except caffeine, colchicine and theobromine, true salts of which are not used in pharmacy). Borax does not precipitate alkaloids in presence of glyc-

erin. The free alkaloids are all, however, soluble in alcohol. Some alkaloids, notably morphine, are soluble in an excess of caustic alkali, but not in the carbonates.

Iodine and Iodides.—The official Compound Solution of Iodine, known as "Lugol's Solution," is a delicate reagent for most alkaloids, precipitating them even in very dilute solutions. The iodides of potassium, sodium or ammonium, alone, are not as delicate, but precipitate from stronger solutions, the precipitates being very bulky in some cases.

Solution of mercuric chloride in excess of potassium iodide, known as solution of iodohydrargyrate of potassium, or "Mayer's Solution," is a very delicate and universal precipitant, precipitating all alkaloids from very dilute solutions, except caffeine, colchicine and theobromine. It acts best in acid solutions, and has been used for the quantitative estimation of alkaloids.

It is found in mixtures when mercuric chloride and potassium iodide are combined in them. Mixtures of this sort with alkaloids or alkaloidal tinctures are not infrequent, but the precipitates with this reagent are all soluble in alcohol, hence none is formed in the presence of a sufficient proportion of spirit.

Double iodide of bismuth and cadmium also forms a delicate, though rare precipitant for alkaloids, and the official solution of mercury and arsenic iodides, known as "Donovan's Solution," also acts in the same manner, less delicately.

Bromine and Bromides act in a manner similar to iodine and iodides, but are much less sensitive, as a rule. Strychnine salts are thrown out of solution by potassium bromide, but the presence of 12 per cent of alcohol redissolves them, as already stated.

Tannic acid, and astringent drugs containing it, also precipitate most alkaloids (in the absence of alcohol), and has been largely used as a reagent for this purpose. In a few cases forms of tannic acid are found in alkaloidal drugs, as cincho-tannic acid in cinchona, in which cases alcohol is required to thoroughly extract the drug, unless a mineral acid be present to replace the tannic acid, as in infusion of cinchona. Combinations of alkaloids with astringents are not unusual.

Other Acids.—Many of the organic acids, as citric, picric, tartaric, gallic, oxalic, etc., and also the inorganic phosphoric acid, form very slightly soluble salts with some alkaloids, and these are liable to precipitation. Alkaloidal salts vary in this respect as do metallic salts, but not as much is known about them. Nearly all the hydrochlorides of the alkaloids are soluble in water, but berberine dihydrochloride is quite insoluble, hence preparations of hydrastis, calumba, and other drugs containing berberine, are liable to form precipitates with this acid. The very slight solubility of quinine citrate, acetate and salicylate should be remembered. Some alkaloids have a reducing action, and reduce mercurous and other salts.

Certain drug extracts are used to disguise the bitter taste of quinine in liquid mixtures—notably licorice and yerba santa. These owe a part of their efficiency to the formation of insoluble compounds with the quinine, and insoluble compounds are tasteless. When sufficient alcohol is present to hold these compounds in solution, the effect upon taste is less marked.

Acacia is precipitated hopelessly by solution of subacetate of lead, but not by acetate of lead. Mucilage of acacia forms a gelatinous mass with ferric chloride and with borax; the former is liquefied by free acid or by alkali citrates and water and the latter by sugar or glycerin. Alcohol in excess precipitates it in a tough, stringy mass, which is not diffusible. Mucilage of acacia becomes sour and acid on standing, unless prevented by the use of chloroform, beta-naphthol, or other preservative agent. It prevents precipitation of metallic salts, alkaloids, etc., under many conditions.

It has been stated that acacia contains an enzyme which causes decomposition of tannic acid and astringent drug preparations in aqueous solution, decomposes some alkaloids, some phenol derivatives, etc. This enzyme is destroyed by boiling the mucilage of acacia.

Acetanilid is quite stable. It slowly develops a yellow or red-colored solution when dissolved in spirit of nitrous ether. It forms a liquid when triturated with phenol, pyrocatechin, resorcin, menthol and thymol, and a damp powder with chloral and antipyrine. It is slowly decomposed by strong solutions of caustic alkalis. With alkali iodides and bromides it forms insoluble compounds.

Acetozone is unstable even in the dry form. In solution (it is only slightly soluble in water or other solvents) it decomposes slowly, liberating oxygen and hydrogen peroxide. It has the usual incompatibilities of oxidizing agents.

Acetphenetidin or **Phenacetin** is ordinarily quite stable. It is decomposed by strong acids or alkalis but it is very unusual to find it prescribed with such. It combines with iodine to form iodophenin and gives colored compounds with oxidizing agents, including spirit of ethyl nitrite, chlorine, chromic acid etc. It liquefies or forms a pasty mass when triturated with phenol, chloral hydrate, pyrogallol or pyrocatechin.

Acetylsalicylic Acid or **Aspirin** is quickly decomposed by water into acetic and salicylic acids. This action is hastened by alkalis. In anhydrous solvents it forms salts with bases, which may be soluble in water but are decomposed by that medium. The calcium, magnesium and potassium salts are so formed, and are soluble in water. Acetylsalicylic acid is rendered more soluble in water by the presence of sodium citrate (four times as much citrate as of the acid for the most soluble combination), ammonium acetate, quinine sulphate, euquinine, antipyrine and iron salts, but it decomposes rapidly in such solutions. It is so sensitive to hydration that it is decomposed by the water of crystallization in other salts with which it may be combined. Thus it is slowly decomposed when it is mixed with dry quinine sulphate or other salts containing water of crystallization. Such mixtures are only suitable for prompt use.

It softens or even liquefies when mixed with acetanilid, antipyrin, acetphenetidin, methenamine, phenolphthalein and salol.

It does not give a color with weak ferric chloride solution unless partly decomposed; then the characteristic color with salicylic acid is obtained.

Novaspirin is soluble in water, but is decomposed therein.

Acids, Organic.—All the organic acids are displaced from their salts by mineral acids, particularly those which are only slightly

soluble in water, as benzoic and salicylic acids, which are easily thrown out of combination and solution by hydrochloric, nitric or sulphuric acids. Excepting acetic acid the metallic salts of organic acids are mostly insoluble, and hence salts of the heavy minerals are generally incompatible with solutions containing organic acids and salts. Many of the organic acids coagulate albumin, a notable exception being gallic acid, which for this reason is more assimilable than tannic acid, and valuable for hemorrhage of the lungs, etc.

Tannic acid, and astringent drugs containing it, precipitate alkaloids, a few glucosides, gelatin, albumin, starch and tartar emetic, and gives an intense black color with iron salts. It also forms precipitates with diluted sulphuric, hydrochloric and arsenous acids, and prevents the blue color of iodine and starch.

Aconitine besides the usual incompatibilities of alkaloids, is easily decomposed by excess of alkalis. It is sensitive to heat, but is safe at temperatures below 80° C. Salts of aconitine, if slightly acid, can be sterilized at 100° C. without injury during one hour.

Albumin and Albuminates.—Albumin has feeble acid properties, and combines with bases to form feeble salts. Both albumin and the salts are decomposed easily by acids, are precipitated by boiling and by alcohol in excess, and by many of the metallic salts. Tannic and picric acids and phenol precipitate albumin and albuminates.

Albumin Tannate, Albutannin, Tannalbin, Tannigen (Diacetyl-tannin) **Tannoform** (Tannin-formaldehyde), etc., are all insoluble compounds of tannin which are easily decomposed by alkalis, and also by heat. When used internally they are presumed to liberate tannin in the intestines, but are not affected by weak acids, as in passing through the stomach. They are rarely mixed with other remedies, unless in powder form.

Alcohol.—Alcohol in excess—usually above 50 per cent—precipitates albumin, gums, and many inorganic salts from aqueous solutions. It is easily oxidized by nitric acid, chromic acid, chlorine, bromine, permanganates, etc. Aldehyde in alcohol is darkened by alkalis. Concentrated mineral acids convert it partly into ethers.

It reduces mercuric chloride to calomel, and combines with chloral hydrate, when sufficiently strong, to form chloral alcoholate.

It is separated from solution by strong solutions of potassium citrate.

Aloe.—Ferric chloride, strong nitric acid and spirit of ethyl nitrite give greenish red or yellow colors with tincture of aloe, depending upon the variety and the strength. Alkalis decompose aloin and render it inert.

Amidopyrin or **Pyramidon** has incompatibilities similar to antipyrin, from which it is derived. It is precipitated by Mayer's solution, by tannic acid, mercuric chloride, alum, iodine and quinine bisulphate. It gives a blue color with nitric or nitrous acid, spirit of ethyl nitrite, ferric chloride and other oxidizing agents. It reduces calomel. It softens when mixed with phenol or chloral hydrate.

Amyl nitrite resembles spirit of nitrous ether (which see) in its properties. It is decomposed by exposure to light, water and air, becoming acid.

Anthrarobin solutions absorb oxygen, and darken; alcoholic solutions slowly, alkaline solutions quickly. It gives a brownish-green color with ferric chloride and a brown precipitate with lead acetate.

Antipyrin, also known as **Phenazone** and **Analgesin** is an artificial alkaloid, and unites with acids as do alkaloids. It is precipitated by the common alkaloidal reagents from strong solutions, such as potassium-mercuric iodide, iodine, bromine, mercuric chloride, tannic acid, alkalis, etc. In some cases precipitation depends upon the strength of the solution, the presence of acid or the proportion of the reagents.

It acts upon calomel in the presence of moisture, darkening it and converting the calomel partly into a mercuric salt. Hence this is a dangerous incompatibility in that a poisonous salt of mercury is formed. This action is stated to be more rapid in the presence of sodium bicarbonate.

It combines with phenol, salicylates and chloral, forming compounds which are usually liquid. It also liquefies when triturated with beta naphthol, resorcin, thymol, methane, pyrogallol, salol, pyrocatechin and piperazine.

It is easily oxidized forming colored compounds. With nitric acid the liquid becomes first yellow, then red. With spirit of ethyl nitrite a green liquid is obtained (quickly if the spirit is acid and slowly if neutral) consisting of iso-nitroso-antipyrine. This compound was formerly thought to be poisonous, but is now known to be safe. With ferric salts a red color is produced, with chlorine a yellow to red, with chromic acid an orange, and with copper salts a green.

It is stated to increase the solubility of caffeine and quinine salts in water, and it destroys the fluorescence of quinine solutions, and prevents the thalleioquin reaction.

It is likely to be thrown out of solution by many very soluble salts, as salicylates, etc., and is generally a troublesome ingredient of complex solutions.

Apomorphine Hydrochloride oxidizes easily in solution, the liquid becoming green or brown. This is hindered by a slight excess of acid in the solution, and is prevented for a considerable time by the presence of a small amount (0.1 per cent) of sulphurous acid or of sodium bisulphite.

It is decomposed by the heat of boiling water, unless stabilized by an excess of acid.

Oxidizing agents produce colored solutions, usually green or red, and alkalis precipitate it, the mixture becoming dark on standing. It is precipitated by the common precipitants of alkaloids.

Asaprol is precipitated by solutions of quinine and antipyrin, and is decomposed by carbonates.

Atropine in the free condition is easily decomposed by heat. Its salts, if strictly neutral or slightly acid, can be sterilized at 100° C. for one hour without injury. Excess of alkali entirely decomposes **Atropine**, **Hyoscyamine** and **Hyoscine** quickly upon heating, slowly in the cold. **Homatropine** has practically the same properties. All are precipitated by the general alkaloid precipitants—tannin, iodine, etc.

Barbital or **Veronal** (diethylbarbituric acid) and **Luminal** or **Phenobarbital** are acid bodies which form soluble salts with alkalis, the latter being more quickly acting because of their solubility. These

are quite stable and are mostly administered alone. They may reduce calomel, and are decomposed by heating with alkalis.

Beta-naphthol liquefies by trituration with antipyrin, camphor, exalgin, menthol, phenol, urethane, and salol. It gives a green color with ferric chloride.

Butyl-chloral is decomposed by alkalis, being converted into allylene dichloride and a formate and chloride of the alkali. It liquefies with phenol, menthol, pyrocatechol and urethane.

Caffeine is not precipitated by alkalis, or the usual alkaloidal reagents, except tannin in strong solutions, and iodine in acid solutions. It is more soluble in citric acid, benzoate and salicylate solutions than in water.

Citrated caffeine in solution, unless very concentrated, splits up into caffeine and free citric acid, and the latter may display its own incompatibilities.

Camphor liquefies when triturated or warmed with chloral, butyl-chloral, menthol, thymol, resorcin, beta-naphthol, salol, urethane, pyrocatechol, pyrogallol, and phenol. The liquid thus formed is soluble in alcohol and oils, but is thrown out of its alcoholic solution by the addition of water. The presence of camphor in Tully's powder should be remembered in this connection. With resins a soft mass is formed. It unites with iodine and bromine, and with gaseous hydrochloric, and sulphurous acids.

Fluid mixtures containing camphor with chloral, phenol, etc., may at first be clear; but if much water is also present the liquefied chloral-camphor, camphor-phenol, etc., is liable to separate the oily drops, which require vigorous shaking to diffuse. Any two of these bodies form a liquid of this character when mixed.

Soluble salts throw out camphor from its aqueous solution—*i. e.* camphor water. On the other hand, sugar, magnesia and carbon dioxide are said to increase its solubility in water.

Camphor, monobromated, liquefies when triturated with chloral, phenol, salol and thymol.

Chloral hydrate liquefies, when triturated with camphor, phenol, thymol, menthol, exalgin, methacetin, phenacetin, salol and urethane. A damp powder results with acetanilid. Aqueous solutions of chloral decompose on long standing, becoming acid in reaction. Chloral is decomposed by alkalis, forming chloroform and formate of the alkali. Bottles containing such a combination, which have been stored in a warm place, have exploded from the pressure of chloroform vapor. This incompatibility of chloral with soda or potassa, or their carbonates, with aromatic spirit of ammonia, borax, lime-water, magnesia, etc., is important to remember. In the presence of alcohol and certain very soluble salts, as potassium and sodium bromides, sodium chloride and magnesium sulphate, the chloral may unite with the alcohol to form *chloral alcoholate*, a liquid which exercises a very harsh and irritating action upon the system. This may remain in solution if enough alcohol is present, may float upon the surface, or may sink to the bottom according to the density of the aqueous solution. This formation does not occur in the presence of ammonium or calcium bromides, ammonium chloride or potassium nitrate.

Chloral slowly decomposes in solution with potassium iodide, liberating chloroform and iodine.

A strong aqueous solution of chloral hydrate dissolves resins, volatile oils, organic acids, some fats, esters, chloroform, and many bodies which are insoluble in water. It is almost a universal solvent, and itself dissolves in most pharmaceutical solvents. Aqueous solutions are slowly decomposed by light,—strong solutions more rapidly than weak.

Chloralamide is also decomposed by alkalis, and by hot water.

Chloralimide is decomposed by mineral acids, forming chloral and an ammonium salt.

Chloramine is alkaline in reaction, and is decomposed rapidly by mineral acids, yielding chlorine. It is decomposed by alcohol, and yields chlorine more slowly in water solution.

Chloretone is decomposed by weak alkalis and should not be dispensed with borax, carbonates, etc. It softens or liquefies when mixed with menthol, phenol, or exalgin.

Cinchophen, also known as **Phenylcinchoninic Acid** and as **Atophan** form salts with alkalis which are soluble in water. It is rarely combined with other medicaments. Salts made with it of the heavy metals are insoluble.

Cinchonidine and **Cinchonine**, when in combination with organic acids and in solution, slowly form **cinchotoxin**, more rapidly when heated. This change is hindered or prevented by mineral acids. (See Quinine.)

Cocaine is a very unstable alkaloid, being gradually decomposed in aqueous solutions particularly if neutral. Preparations containing cocaine do not keep well, the alkaloid gradually hydrolyzing, and for this reason preparations of coca have been dropped.

Cocaine acts as a reducing agent, blackens calomel and reduces other mercurous salts, forming some mercuric salt.

Solutions of cocaine hydrochloride may be sterilized at 100° C. for one hour if slightly acid, but are partly decomposed if a trace of alkali is present. Cocaine is decomposed by strong mineral acids and reduces calomel. The synthetic substitutes for cocaine, which include **Alypine**, **Anesthesin**, **Apothesin**, **Benzocaine**, *alpha* and *beta* **Eucaïne**, **Holocaine**, **Nirvanine**, **Novocaine**, **Orthoform**, **Tropocaine**, **Stovaine**, and **Subcutin** are all more stable than cocaine, are less easily affected by heat and are more permanent in solution. Novocaine appears to change in some way in solution that produces dangerous physiological effects. Only fresh solutions should be used.

Codeine is more soluble, as a free alkaloid, and more strongly alkaline than most alkaloids. It is hence less easily precipitated by alkalis and under favorable conditions it may itself precipitate metallic salts or other alkaloids, as do alkalis.

Colchicine decomposes easily in aqueous solutions, particularly in the presence of alkalis, or strong acids. It is precipitated by the general alkaloidal reagents, particularly iodine solutions.

Collodion.—The pyroxylin in collodion is partially reduced by alkalis, yielding a product which is soluble in weakened alcoholic solutions. Water precipitates it. Also phenol.

Coniine is not precipitated by alkalis, but it precipitates metallic salts.

Creosote is readily oxidized by nitric acid and other oxidizing agents. It is liable to inflame if mixed suddenly with these. Its aqueous solution reduces many salts. It precipitates albumin and some gums and gives colored solutions with ferric chloride.

Creosote carbonate is decomposed by alkalis. In other respects it has the properties of creosote.

Cresol is used mostly in alkaline soap-solutions (as creolin, lysol, etc.), which are therefore incompatible with acids, or in acid solution (as sulpho-naphthol, etc.), which are incompatible with alkalis. These are seldom mixed with other bodies.

Dermatol is decomposed by strong or hot mineral acids.

Digitalin and digitalis preparations are decomposed by strong alkalis and acids, and are precipitated by tannic acid.

Epinephrin, also known as **Adrenalin**, **Suprarenin** etc. is a basic body which combines with acids. It is extremely sensitive to oxidizing agents, which decompose it. This decomposition is shown in a change of color, usually to a red, then to brown. The change is hindered by strong acids, less so by weak acids, and is hastened by alkalis. Solutions of epinephrin must be acid to be stable, but even then exposure to the air will oxidize it. Even the weaker oxidizing agents, such as ferric salts (in minute quantity) arsenic solutions, mercuric chloride, iodine, etc., cause decomposition in a few hours. It gives brightly colored solutions with many of the oxidizing agents, such as a green with ferric salts, blue with bichromates, red with iodine, pink with manganese dioxide, etc. The colors are changed by the addition of acids. It is so sensitive to change that it should be combined with other medicaments cautiously, and preferably in quantities only sufficient for a very few days use at a time.

Ergotin is decomposed by heat, and is precipitated by alkalis, tannin, iodine, and most of the alkaloidal reagents.

Europhen is decomposed by hot liquids and by light. It is incompatible with metallic oxides, and mercury salts, and with starch in the presence of fats—as in ointments. It is slowly decomposed by fats and oils.

Exalgine (methyl acetanilid) yields a pasty mass when triturated with salicylic acid, but remains dry with sodium salicylate. It forms a liquid with beta-naphthol, chloral, menthol, phenol, pyrogallol, resorcin, salol, salicylic acid, thymol, euphorin, urethane.

Formic Aldehyde (Formalin) slowly deposits the crystalline paraform, more rapidly if heated below 80° C. It unites with ammonia, forming an odorless solid, and is decomposed by alkalis, which are neutralized. It forms insoluble compounds with albumin, gelatin, cocaine starch, etc., which are not usually stable. It is a powerful reducing agent, and is incompatible with proflavine and with all oxidizing agents. Iodine, hydrogen peroxide, etc., oxidize it to formic acid, which is very irritating.

It unites with sulphides and with alkaline sulphites.

Gelatin is rendered insoluble in water by chromic, picric and tannic acids, chlorine water, mercuric chloride, alcohol, alumnol and formaldehyde. Its solution in glycerin, without water, is less affected by these agents. Long heating, and acids or mineral salts, slowly destroy its gelatinizing properties.

Glucosides are decomposed by mineral acids, ferments and by hot water. Alkalis may decompose them. Tannic acid precipitates most of them.

Glycerin, when undiluted, is liable to form an explosive compound with strong nitric, nitrohydrochloric, or chromic acids. When diluted, all oxidizing agents decompose it, usually forming oxalic acid and carbon dioxide. Prof. LaWall states that a mixture of glycerin and hydrogen dioxide is stable for some days.

It is an excellent solvent for the water-soluble sulphates (which are mostly insoluble in alcohol), for borax—which it renders acid in reaction—for some of the metallic oxides, notably lead monoxide, for many of the organic acids and other bodies which are only slightly soluble in water. It prevents precipitation of salts, alkaloids and other bodies in many cases. It is therefore a useful agent in pharmacy to prevent precipitation of bodies that may otherwise be thrown out by reaction or from physical causes. It is not a solvent for oils, camphors, resins, etc., but may prevent their precipitation from alcoholic solutions in the presence of a limited amount of water.

Glycyrrhizin is precipitated by acids. It precipitates some metallic salts.

Glyceryl Nitrate is decomposed by alkalis, and by water. The latter very slowly.

Guaiacol and **Guaiacol carbonate** have incompatibilities corresponding to creosote and creosote carbonate.

The other derivatives of guaiacol—**Duotal** (guaiacol carbonate, Heyden), **Benzosol** (guaiacol benzoate), **Styracol** (guaiacol cinnamate), **Monotal** (guaiacol methylglycolate), **Guaiacol-salol**, etc.—are all insoluble in water and are decomposed by alkalis.

Hydrogen Peroxide is decomposed by shaking and rapid heating. It is more stable in the presence of acids, and its solution is slightly acid in reaction. Alkalis and metals decompose it quickly. It is an active oxidizing agent and reacts with all oxidizing and reducing agents, alcohol, albumin, etc. It liberates iodine from iodides, and is itself decomposed by admixture with most substances except a few neutral salts. It is usually, and best, prescribed alone.

Ichthyol, also **Sulphonated Bitumen**, are precipitated by strong acids and by alcohol. Alkalis liberate ammonia, but do not precipitate it as a rule. Sometimes cloudy solutions are formed. It is precipitated by many metallic salts, and in part by some of the alkali salts particularly from strong solutions. It precipitates alkaloids from solutions of their salts, forming sticky masses. On the other hand it aids the solubility in water of creosote, guaiacol, eucalyptol, camphor and some volatile oils.

Infusions and Decoctions are immiscible with alcoholic tinctures and preparations containing resinous or oily matter. They are decolorized by solution of subacetate of lead and sometimes by acetate of lead. Precipitates, due to astringent principles, organic acids, etc., are likely to form when corrosive sublimate, tartar emetic, silver salts, iron salts, etc., are added to infusions or decoctions. Those containing alkaloids form insoluble alkaloidal tannates when mixed with astringent preparations, as tinctures of kino and catechu.

Iodoform is decomposed by light and heat and by alkalis. This and many kindred bodies,—**Diiodoform**, **Aristol**, **Iodine Trichloride**, **Iodophenacetine**, **Europen**, **Iodoformin**, **Iodol**, **Losophan**, **Nosophan**, **Loretin**, **Isoform**, **Vioform**, **Sozoiodol**, etc., owe their antiseptic properties to the looseness with which they hold iodine, and are more or less easily decomposed by organic matter and salts; hence they should not be mixed with bodies having a strong affinity for iodine, as alkalis, volatile oils, silver salts, etc. Water, fats, tannin and oxidizing agents all decompose iodoform more or less rapidly, particularly in the light.

Menthol liquefies when triturated with beta-naphthol, camphor, chloral, exalgine, phenol, pyrogallol, resin, resorcin, thymol and urethane.

Mercurochrome is soluble in water and in alkaline solutions, but is decomposed by acids, which precipitate mercury compounds. It is thrown out of solution by many soluble salts, all acid salts, and forms insoluble compounds with many alkaloidal salts.

Methacetin liquefies in contact with chloral and phenol, and forms a damp powder with resorcin which dries on standing.

Methenamine or **Hexamethylenamine**, also known as **Urotropin**, **Formin**, **Uritone**, etc. is alkaline in reaction and forms salts with weak acids, such as saccharin, phenolcinchoninic acid, barbituric acid etc.

Mineral acids, and the stronger organic acids decompose it, liberating formic aldehyde and forming a salt of ammonia.

This action is rapid with inorganic acids but slow with organic. It slowly precipitates morphine from solution but does not precipitate other alkaloids unless in strong solution. It combines with alcohol in presence of hydrochloric acid forming acetal. Similar combinations are formed with phenol, guaiacol, eugenol, etc. It slowly darkens with ammonia salts. It is precipitated by tannic acid and by mercuric chloride and combines with gelatin, rendering the latter insoluble. Hence it is not suitable for dispensing in gelatin capsules. It liquefies when triturated with acetylsalicylic acid. Tablets of hexamethylenamine burn quietly with a non-luminous flame and are handy for heating small amounts of liquid or small instruments.

Methylene Blue is incompatible with reducing agents, with strong alkalis, and with potassium iodide.

Morphine is precipitated by alkalis, but is redissolved by solutions of the caustic alkalis and by lime water. It is but slightly soluble in alcohol, and its precipitation is usually not prevented by this body or by glycerin. It reduces oxidizing agents, and is decomposed by them.

Morphine acetate loses acid and becomes colored when its solution is heated, hence it cannot be sterilized by heat. The other salts of morphine can be heated to 100° for an hour or more without injury but are likely to discolor if a trace of alkali is present. The derivatives of morphine, which include **Apomorphine**, **Dionine** (Ethyl-morphine), **Heroine** (Diacetyl-morphine) and **Peronine** (Benzylmorphine) are all more sensitive to heat than morphine, and should not be heated to 100° C. in solution. Apomorphine is very sensitive to light, becoming green. This discoloration can be prevented by the addition of a small amount of sodium bisulphite. The derivatives are more soluble in

alcohol, chloroform, etc., than morphine and are less easily precipitated by alkalis. On the other hand they are decomposed by alkalis.

Naphthalin liquefies in contact with phenol and salol.

Oils.—Fixed oils are saponified by alkalis, by metallic oxides and solution of lead subacetate, and sometimes by strong acids. With strong nitric acid some of them form a yellow solid body, called *claidin*. Iodine combines with them in the cold and sulphur when hot. Contact with aqueous fluids and with metals causes them to become rancid more rapidly.

With the exception of castor oil (and croton oil, slightly soluble), they are insoluble in alcohol.

Volatile oils are incompatible with nitric acid and strong oxidizing agents. Bromine and iodine react violently with many of them and, form compounds with all. Very soluble salts throw out the volatile oils from their aqueous solutions, as in the aromatic waters. Water and saline solutions also separate them from alcoholic solutions. Many of the volatile oils give color reactions with tincture of ferric chloride.

Pancreatin has its action impaired by acids, while *Pepsin* acts well only in acid solutions. It is precipitated in flocculent condition by alcohol and by tannin. Heat above 70° C. renders it inert.

Papoid is active in both acid and alkaline solutions. It is injured by heat, and precipitated by agents that precipitate albumen.

Paraldehyde is a strong reducing agent. It unites with alkali hydroxides to form a resinous mass. It is said to liberate iodine from iodides.

Pepsin has its digestive activity seriously reduced by the least trace of alkali, by strong agitation when in solution and particularly when a little above the normal room temperature, by strong acids, by strong salt solutions and by more than about 25 per cent of alcohol. It is most stable in solution when very slightly acid—equivalent to about 0.03 to 0.05 per cent hydrochloric acid, and containing less than 25 per cent of alcohol.

Agents which precipitate albumin, such as tannin, phenol, mercuric salts, heat above 70° C., etc., will precipitate pepsin.

Phenocoll Salts are decomposed and the base precipitated by alkalis and carbonates of the alkaline earths. It is precipitated by mercuric chloride, ferric chloride, silver nitrate and tincture of iodine.

Phenol (Carbolic acid) forms a liquid when in contact with acetanilid, antipyrin, beta-naphthol, camphor, monobromated camphor, chloral, exalgin, menthol, methacetin, naphthalin, phenacetin, pyrogallol, resin, resorcin, salol, thymol, urethane, methenamine, vanillin, santonin, pyramidon, caffeine and many alkaloids. It combines with the alkali hydroxides to form carbolates. It combines with strong sulphuric acid, forming sulphocarbolic acid. It precipitates collodion, also gelatin and albumin from aqueous solutions. Alcohol neutralizes its caustic qualities. It gives a blue color with ferric chloride. Oxidizing agents change it in various ways.

Phenolphthalein, partly on account of its slight solubility in water, and partly because of its unpleasant taste, is rarely prescribed in solution. It is acid in reaction and turns red with alkalis, which also make it soluble. It is soluble in glycerin and in alcohol. Reducing agents change its color in alkaline solutions.

Physostigmine or **Eserine** is one of the most sensitive of the alkaloids, easily decomposed by even the weak alkalis. Its solutions become red on exposure unless an excess of acid is present.

It is easily decomposed by heat, and its solutions cannot be sterilized by this means. Even a heat of 60° C. partially destroys it. Most of the salts are deliquescent and thus are more liable to discolor.

Pilocarpine has the usual incompatibilities of alkaloids. It is not as readily precipitated by alkalis from dilute solutions as are most alkaloids. It darkens calomel.

Piperazin has an alkaline reaction which causes it to precipitate substances that are thrown out of solution by alkalis. This will not occur if the piperazin be first neutralized with acid. It acts in some measure as an alkaloid, and is precipitated by the more active alkaloidal reagents. It is a reducing agent. It liquefies when triturated with acetanilid, antipyrin, phenol, chloral hydrate or phenacetin.

Pyoktannin is decolorized by strong light, in solution, and is precipitated and decomposed by strong alkalis. Excess of neutral salts throw it out of solution.

Pyrocatechin has, in general, the incompatibilities of resorcin.

Pyrogallol is a powerful reducing agent, acting upon solutions of mercury and silver salts in the cold. Its aqueous solution absorbs oxygen from the air and darkens, particularly if alkaline. Oxidizing agents and alkalis give various colors with it in aqueous solution. It forms a soft mass or liquid when triturated with antipyrin, camphor, carbolic acid, exalgin, menthol, pyrocatechin, urea or urethane.

Quinine salts are precipitated by acetates (usually not by acetic acid, unless very dilute), benzoates, citrates, salicylates and tartrates, by strong solutions of iodides and by the usual alkaloid reagents. Some of the salts are less soluble in strongly acid than in weakly acid solutions. The fluorescence of quinine sulphate in weak sulphuric acid solution is destroyed by hydrochloric acid and chlorides, bromides and iodides in dilute solution (strong solutions precipitate the quinine), by hypophosphites, by alkali citrates in excess, and by acetanilid, antipyrin, phenacetin and piperazin.

Salts of quinine with organic acids, as the acetate, citrate, salicylate, etc., slowly change in aqueous solution forming **quinotoxin**—or **quinicine**. This change takes place rapidly when heated, hence solutions of these salts cannot be sterilized by heat. The action is hindered or largely prevented by mineral acids. This incompatibility should be carefully guarded against.

Mixtures of quinine sulphate with acetylsalicylic acid slowly react, the water of crystallization in the quinine sulphate decomposing the acid to form acetic and salicylic acids, and these in turn act upon the quinine, forming quinicine. The mixture becomes pasty and darkens in color, and therefore is not suitable for stock preparations. Such a mixture is very common in prescription practice, but should always be recently prepared. It is not suitable for tablets.

Quinicine (or quinotoxin) is reported to have toxic properties, producing a rash on the skin, nausea, some fever, and in severe cases death by convulsions. Dr. Ruddiman has tried the above mixture upon rabbits and guinea pigs and failed to obtain any marked toxic

action. The frequency of the use of this mixture by physicians indicates either that the reaction is too slow to produce unpleasant results or that the reactive products are of very low toxicity. Yet some think that it is often sufficient to produce the rash and increase the fever in cases of influenza, etc.

The salts of quinine with mineral acids may be sterilized at 100° C. without injury.

Quinine sulphate gives a damp mass with resorcin, thymol and with chloral hydrate. Antipyrine, ammonium chloride, and potassium nitrate increase its solubility in water.

The compounds of quinine, as **Aristochin** (Diquinine Carbonate), **Euquinine** or **Quinine Ethylcarbonate** and **Neoquinine** (Quinine Cinamic Ester) are all insoluble and are generally miscible with other bodies. Mineral acids liberate the quinine and dissolve them.

Resins.—Alkalis dissolve most resins, forming soaps with them. Strong oxidizing agents decompose them. An alcoholic solution of hydrochloric acid gives a colored solution with many resins which is characteristic. Most resins soften or liquefy when triturated with camphor, menthol, phenol, thymol and salol.

Resorcinol darkens on exposure to air, more rapidly in solution and in the presence of alkalis. It gives a bluish color with ferric chloride and with hypochlorites. Ethyl nitrite produces a red color. It makes a liquid or soft mass with antipyrin, camphor, chloral, phenol, menthol, quinine and some others. Aqueous solutions of resorcin dissolve camphor, etc.

Saccharin or **Gluside**, or **Benzosulphinide**.—The aqueous solution is acid in reaction and neutralizes alkalis. It forms agreeable compounds (salts) with alkalis, and dissolves some metallic oxides, as zinc and magnesium oxides. The salts are called saccharinates, but more correctly are sulphamidobenzoates. The best sweetening effects are produced by the sodium salt which is neutral in reaction. Excess of alkali decomposes saccharin, in solution.

Salicylic acid forms a liquid with exalgin and urethane. Sodium salicylate remains dry with these. (See salicylates.)

Salol or **Phenyl Salicylate** is readily decomposed by alkalis and precipitated by bromine water. It forms a fluid when triturated with camphor, monobromated camphor, chloral, naphthalin, phenol, resin, thymol, and urethane.

J. R. Wotring finds that one part of salol with two parts of menthol produces a dry powder, but two parts of salol with one of menthol liquefies, and equal parts of the two give a damp powder.

Salol liquefies with camphor in all proportions. Salol with antipyrin, acetanilid or phenacetin gives dry powders, but if camphor be added a paste or liquid results. One part of salol with two of chloral gives a moist powder, but most proportions give a liquid. Salol may be mixed with acetanilid to obtain a dry powder, but if antipyrin be added a liquid results.

With either antipyrin or resorcin it makes a dry powder, but if all three are mixed a pasty mass is obtained. (See Eutectic Mixtures p. 240.)

Salol does not powder easily when triturated in a mortar, becoming sticky when rubbed. It is best powdered by moistening with a trace

of oil—only a trace being needed. It is suspended in mixtures by dissolving in ether and triturating this solution with powdered acacia or tragacanth, then allowing the ether to evaporate and treating the powder with the liquid.

Salophen gives a violet color with tincture of ferric chloride. Potassium hydroxide aids its solution in water, but decomposes it.

Santonin darkens on exposure to light, and dissolves in alkaline solutions, forming santoninates. These salts are more active and poisonous than santonin, and must be administered cautiously. It precipitates salts of lead, iron and copper, and is precipitated by tannic acid and by chlorine.

Soaps are decomposed by acids, alkaline earths, and mineral salts. The latter are precipitated as insoluble soaps. Soaps are insoluble in hard waters until after the mineral matters in the water have been precipitated.

Spirit of Nitrous Ether, when neutral and undecomposed, has no important incompatibilities, but may be thrown out of solution by soluble salts when used liberally. This effect resembles an effervescence, because the boiling point of ethyl nitrite is so low (about 61° F.) that it immediately volatilizes and passes out of the liquid as vapor. This neutral state is an ideal condition, however, which is rarely ever realized, and never to be trusted. Light and water decompose it, liberating nitrous acid, which causes many troublesome reactions. The decomposition commences as soon as made, and proceeds more or less rapidly according to the exposure, the temperature, and the proportion of water present. With strong alcohol, containing 5 to 6 per cent of water, the decomposition is very gradual. The spirit becomes acid, then it loses its fragrant odor and becomes unpleasantly pungent, then it darkens.

The acid causes an effervescence with carbonates, neutralizes alkalis, and acts as an oxidizing or a reducing agent according to conditions. It liberates iodine from iodides and bromine from ammonium bromide. Other bromides are not easily decomposed by it (Ruddiman). It oxidizes hypophosphites and sulphites, and reduces chlorates, chromates and permanganates. It produces a green solution with antipyrin and with thymol (green or brown), a yellow with acetanilid and with morphine, a red-brown with salicylates and phenols. Mercurous salts (calomel, etc.) and mercuric salts are reduced.

With tannic and gallic acids, and some other organic bodies, it reacts slowly, giving off gaseous compounds consisting chiefly of nitrogen oxides. This reaction is usually slow and troublesome, and occurs with combinations of nitrous ether with fluid extracts of buchu or uva ursi, tincture of cubeb, and others. Very soluble salts, in fairly concentrated solution, throw nitrous ether out of solution in alcohol, and it volatilizes rapidly, producing the effect of an effervescence.

All these incompatibilities except the last can be prevented by rendering the spirit of nitrous ether permanently neutral with alkali, but the nitrous ether is then decomposed into a nitrite and ethyl alcohol.

Strychnine salts are more easily precipitated than most alkaloids, and they frequently separate only after several hours. Very slight amounts of alkali are sufficient to precipitate strychnine, and arsenites

bromides and iodides, as well as some chlorides, throw strychnine out of solution, sometimes as the original salt, sometimes as another salt. Strong solutions of very soluble neutral salts are liable to precipitate strychnine sulphate from solution. Alcohol tends to prevent the precipitation. Since strychnine is very sensitive to all alkaloidal precipitants, and tends to separate slowly from solution, a shake label is frequently advisable on strychnine mixtures, unless 15 per cent or more of alcohol is present.

Sugar solutions form soluble saccharates with lime, magnesia, litharge, and other metallic oxides. Hence syrup tends to prevent the precipitation of metallic salts as oxides or hydroxides. Heated with borax it liberates boric acid in a manner similar to glycerin. Many incompatibilities are hindered by syrup, partly by its viscosity and neutral character hindering chemical action. Mineral acids and metallic salts invert cane sugar, slowly in the cold, rapidly when heated.

Heat, with mineral acids or mineral salts, causes a darkening of the sugars. Hence the darkening of syrup of hydriodic acid. Organic acids act similarly but less actively. Strong oxidizing agents decompose sugar, causing explosion if rubbed together in a dry condition, or proceeding quietly in solution.

Milk sugar, in alkaline solution, reduces salts of silver, mercury or copper.

Sulphonal is a very stable body, unaltered by most reagents.

Takadiastase is precipitated by strong alcohol and its action inhibited. Alcohol of 30 to 70 per cent will destroy it in time. Its action is also inhibited by acids and alkalis, in more than traces, and by metallic salts.

Terebene resinifies and becomes acid on exposure to light. It is readily oxidized by exposure to the air and by oxidizing agents. It combines actively with chlorine, bromine and iodine, forming addition compounds.

Theobromine.—This alkaloid resembles caffeine, in its relations to acids—not forming salts easily—but is less soluble in water. It also resembles morphine in its property of dissolving in solutions of fixed alkalis but not in ammonia. It forms double salts which are very soluble in water. Such salts are **Theobromine Sodio-salicylate** or **Diuretin**, **Theobromine Sodio-acetate** or **Theocin**, also **Agurin**, **Theobromine Sodio-citrate** or **Urocitral**, **Theobromine Sodio-formate** or **Thephorin**, **Theobromine Lithio-benzoate** or **Uropherin B**, **Theobromine Lithio-salicylate** or **Uropherin S**. etc. These are all alkaline in reaction and are soluble in water but are decomposed by weak acids and the theobromine is precipitated. Even carbon dioxide will decompose some of these, hence old salts are likely to be insoluble through absorption of carbonic acid. This is corrected by addition of sodium hydroxide. Weak organic acids and bicarbonates, precipitate theobromine from these solutions as well as acids of all kinds, unless in marked excess. Aromatic spirit of ammonia, solution of ammonium acetate, and neutral ammonium salts also precipitate theobromine by liberation of ammonia gas through reaction with the fixed alkali present in the compounds. Salts of other alkaloids act similarly, either theobromine or the alkaloid being precipitated. Iodine solutions precipitate it in absence of alcohol or excess of alkali.

Thiol is precipitated from aqueous solutions by acids, strong alkalis, and mineral salts.

Thiosinamine is decomposed by water, but this change is limited by the presence of glycerin. Freshly made solutions only should be used.

Thymol is a phenolic body which unites with alkalis to form compounds which darken on exposure to air and light and are mostly soluble in water. It combines with iodine in alkaline solution, yielding insoluble thymol diiodide. Oxidizing agents produce colored compounds, as a green or brown with spirit of ethyl nitrite, a blue or blue-green with nitric acid, etc. It reduces some salts, especially in the presence of alkali. It forms eutectic mixtures with a number of bodies which are liquid or soft at ordinary temperatures,—such as with acetanilid, antipyrine, caffeine, camphor, monobromated camphor, chloral hydrate, euphorin, exalgin, menthol, methenamine, phenol, pyramidon, pyrocatechin, quinine salts, resins, salol, santonin, urethane and vanillin. Glycerin is said to aid its solution in water.

Trional is very stable. It liquefies when rubbed with chloral hydrate or salol.

Urethane is decomposed by caustic alkalis. It liquefies with antipyrin, camphor, chloral, euphorin, exalgin, menthol, naphthol, phenol, pyrocatechin, pyrogallol, resin, resorcin, salicylic acid, benzoic acid, salol and thymol (Ruddiman).

THE FORMATION OF A GAS.—This may be known in one of three ways—by an effervescence, by an explosion, or by a combustion. The first two differ only in degree, an effervescence being the bubbling of a gas through a liquid, occurring when free escape of the gas is allowed, and an explosion being the sudden and forcible escape of gas, either from a gradually accumulated pressure within a confined space which at last became powerful enough to burst its container, or from a sudden reaction between two concentrated chemicals whereby a large volume of gas is formed instantaneously.¹

Combustion occurs when a gas rich in oxygen is liberated in the presence of an easily combustible body, the latter catching fire.

Effervescent incompatibilities are troublesome only when the effervescence is slow. When it is prompt the general directions given on pages 53 and 54 should be followed, as the incompatibility is intentional in most of such cases.

A very slow effervescence may be due to two causes—(1) the slow escape of gas from a very viscid liquid, or (2) the slow union of chemicals having weak affinities. Instances of the first are found in reactions occurring in the presence of syrups or of glycerin.

Thus syrup of squill is sometimes combined with a carbonate, and the weak acetic acid in the syrup causes the evolution of carbon dioxide from the latter, but owing to the weakness and viscosity of the acid solution the reaction is very slow and persistent. It may be hastened by heating gently, or by making the syrup extemporaneously, *i. e.*, taking an equivalent of vinegar of squill to which

¹ Explosions may also occur from *physical* causes, as the partial vaporization by heat of very volatile bodies, such as stronger water of ammonia, ether, benzine, etc., confined in tightly stoppered bottles, or other closed containers. Explosions due to chemical causes only are considered in this chapter.

the carbonate is first added, and when the reaction (which will be prompt) has ceased, adding the proper amount of sugar and water.

Dobell's solution is sometimes ordered without any water, only glycerin, borax, bicarbonate of sodium and phenol being used, and a strong solution thus made, which is afterward diluted. If these be mixed cold, the reaction does not start promptly, and may continue for several hours. It should be hastened by using a part of the glycerin at first, which is heated with the borax and bicarbonate, and when the reaction has ceased the phenol and the rest of the glycerin are added.

But reactions may be slow owing to purely weak affinities, and in these cases but little can be done. Such are mixtures of bismuth subnitrate and sodium bicarbonate with liquids, the bismuth being gradually reduced and liberating nitric acid, which then reacts with the bicarbonate; also mixtures containing spirit of ethyl nitrite and tannin, or other bodies which gradually decompose the nitrous ether, liberating oxide of nitrogen. To hasten the reaction in such cases is simply to hasten the decomposition of a desired body, and it therefore should be hindered as much as possible, rather than hastened. To guard against an explosion the stopper should not be pressed tightly into the neck of the bottle, and the customer should be warned of a probable change in the mixture. Such mixtures are usually prescribed in small quantities, that they may be frequently renewed if desired.

Explosions and combustions are caused for the most part by violent chemical action, and are more liable to occur during the compounding than afterward.

They are due to a reaction between an oxidizing and a reducing agent.

Oxidizing agents are chemical bodies, rich in oxygen, which under favorable circumstances part with some or all of their oxygen, the latter immediately combining with another (reducing) body.

Reducing agents are those which are capable of combining readily with oxygen, and are therefore bodies which burn easily; or they may be bodies which are raised from a lower to a higher valency by the action of an oxidizing agent. In all reactions occurring between oxidizing and reducing agents, there is a parting with oxygen on the one hand—the oxidizing agent being thereby reduced—and a combining with the same oxygen on the other hand—the reducing agent being thereby oxidized. When these reactions occur between dry bodies they are usually accompanied by heat and flame and a detonation; when they occur in liquids, heat and sometimes flame accompanies them, but usually no detonation.

These reactions occur in liquids spontaneously, but in solids they take place only when heated. It is well known that solids burn only when they are heated to a certain temperature called the "critical point," and so oxidizing and reducing agents may be mixed without any reaction occurring, provided the temperature is kept below the "critical point," and this is true, in a measure, of liquids as well as solids.

Heat is produced by friction, hence if an oxidizing and a reducing agent be *rubbed* together, as in a mortar during the process of mixing, a reaction is liable to ensue, and this reaction may be so violent as to result in an explosion with serious injury to the operator.

Mixtures of this character are, however, frequently called for in pharmacy, and can be dispensed without danger if properly handled. The invariable rule to be followed in the case of solids is to *powder each ingredient separately, then transfer to a sheet of clean paper and mix with a spatula, avoiding pressure.*

The powders may be mixed by sifting if desired, several siftings being necessary, and friction avoided.

Since the explosion is caused, not by the decomposition of a single body, but by a reaction between two bodies, the powdering of each alone may be accomplished safely; but if the same mortar be used for both substances, all traces of the first must be removed before the second is placed in it.

In the case of liquids which are liable to inflame, this may be prevented by *keeping them cold and mixing slowly.*

A partial oxidation is inevitable in these cases, but a rapid combustion may be prevented.

If the reaction becomes too active it may be checked by cooling with ice water or other suitable means.

Serious injury and even death have resulted to pharmacists in many cases from carelessness in mixing such.

In the following table all the oxidizing agents are incompatible with the reducing agents, the more important and powerful being in heavy type. These should be memorized, and if combined in any mixture, should be mixed with due regard to the precautions already mentioned.

Hydrogen peroxide is peculiar in that it acts both as an oxidizing and as a reducing agent. It reduces oxidizing agents and is itself reduced at the same time, hence is incompatible with all the bodies mentioned in the table. Nitrites may act in the same way, under favorable circumstances.

OXIDIZING AGENTS	REDUCING AGENTS
Arsenates. Chlorates. Hypochlorites. Chlorine and Oxides of Chlorine , including Nitrohydrochloric acid. Bromine and Iodine. Bromates and Iodates. Chromates , including chromic acid and bichromates. Nitrates (nitric acid). Nitrites (sometimes). Permanganates. Peroxides , including hydrogen, sodium and barium peroxides, etc. and lead and manganese dioxides. Silver oxide. Sulphuric acid (with organic matter). Persulphates. Ferric, mercuric and cupric salts. Gold and platinum hydroxides.	Arsenous acid. Cyanides. Phosphorus and Hypophosphites. Sulphur. Sulphides. Sulphites. Hyposulphites. Nitrites (sometimes). Oxalates. Pyrogallol. Ferrous, mercurous and stannous salts. Powdered iron and zinc. Organic bodies , including alcohol, glycerin, ethers, tannins, sugars, adrenalin, paraldehyd, pyrogallol, alkaloids, vegetable drugs, charcoal, cork, syrups, extracts, volatile and fixed oils, pyroxilin, creosote, etc. Hydrochinon. Hydroxylamin hydrochloride. Formic aldehyde.

Among the most common combinations of these are:

Chlorates of potassium or sodium with tannins and sugar for throat troubles, or with sulphur or sulphides. These are par-

ticularly liable to explode with friction, since chlorates part with their oxygen very easily, yielding it up on the application of heat alone.

Chlorates are sometimes prescribed with tincture of chloride of iron and glycerin, for throat troubles. In this case the free hydrochloric acid in the tincture acts upon the chlorate, liberating a highly explosive gas, euchlorine, and unless considerable water is also present an explosion results should the temperature rise as high as 70° F., a common temperature in summer or heated rooms.

This gas is also formed with other mineral acids.



The other oxides of chlorine, as nitrosyl chloride, NOCl, which is found in nitrohydrochloric acid, are also powerful oxidizing agents, and in many cases free chlorine itself. Explosions with these are best prevented by the presence of a considerable proportion of water.

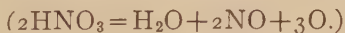
Chlorates are also incompatible in acid solutions with iodides, as potassium iodide, syrup of iodide of iron, etc., the poisonous iodate being formed. With the iron iodide, oxidation to the ferric condition may also occur and free iodine be liberated. Such combinations are inadmissible.

Iodates and bromates act in a manner corresponding to the chlorates, but their use is very rare.

Nitrates, particularly nitric acid, are frequently used as oxidizing agents in the preparation of salts and compounds. Potassium nitrate is one of the principal ingredients of gunpowder, and nitroglycerin is a familiar explosive obtained by the action of nitric acid upon glycerin.

The most common explosive combinations of nitric acid are with oil of turpentine or other volatile oil, creosote, etc. These mixtures should be made in capacious open vessels, the nitric acid being added slowly and the liquids kept cool. Such mixtures, manipulated in this way, are liable to burst into flame, but do not detonate.

In playing the part of an oxidizing agent the nitric acid is split up into water, nitric oxide and oxygen, the latter two bodies acting directly as oxidizers.



The nitric oxide becomes further oxidized to nitrogen tetroxide, NO₂ (or N₂O₄), on exposure to the air, a dense brown and irritating fume arising which is obnoxious in the store or laboratory, hence all mixtures in which nitric acid is reduced should be made in the open air or under a hood.

Nitric acid dropped upon the skin forms the yellow xanthoproteic acid, and a similar yellow is produced upon corks or vegetable matter.

Sawdust has been set on fire by spilling strong nitric acid upon it. *Ous* salts are oxidized into *ic* salts by the acid.

Silver nitrate is reduced in solution in aromatic waters (rose water, etc.), by the volatile oil present. Special care must be exercised in making pills of silver nitrate or oxide to avoid reduction by organic matter. Solutions of silver salts should always be dispensed in bottles protected from the action of light.

Nitrites sometimes act as oxidizing agents, sometimes as reducing agents. In themselves they are prone to change to nitrates and are unstable.

Spirit of ethyl nitrite is perhaps the most troublesome, this being decomposed by light and by water, with liberation of nitrous acid, which changes finally to nitric acid.

Nitrous ether is particularly easily decomposed by tannin, acids and alkalis, liberating gases which may burst the container, if tightly closed. The free acids in the spirit cause effervescence with carbonates, and the liberation of iodine from iodides. These reactions may be hindered by neutralizing the acid before mixing, with a little potassium bicarbonate or carbonate, when no reaction occurs until the ether has become again decomposed by light or other means.

An excess of alkali should never be used, because this immediately decomposes nitrous (and all compound) ethers, forming alcohol and a nitrite of the alkali base.

Chromic acid is a powerful oxidizing agent, causing alcohol, glycerin, and many similar bodies to burst into flame or explode by mere contact. It also acts as a caustic upon the skin, causing painful sores. Bichromates, in the presence of mineral acids, act in the same way as chromic acid. They are used, without the mineral acids, much more frequently than chromic acid.

Permanganates rarely cause explosions. Potassium permanganate acts somewhat slowly but strongly upon such bodies as glycerin, oils, alcohol, and organic matter in general, and is largely used as a deodorizer and purifier. Its disinfectant action is accomplished only when its solution is in contact with the body to be deodorized, the decaying matter being oxidized or burned up by it. Solutions of permanganates should be protected from the light.

Silver oxide is often prescribed in pill form, and explosions have occurred from triturating it with organic matter. Occasionally, pills containing it have exploded several hours after being made. It also forms a very explosive compound with ammonia water and ammonium salts.

Peroxides rarely cause explosions, but like permanganates act slowly and strongly. Peroxide of hydrogen is in itself unstable, and so acts more energetically. It is seldom used in combination with other bodies.

Iodine sometimes causes explosions when added to volatile oils. It combines with these, and less energetically with fixed oils, forming addition compounds.

It is used in analytical chemistry for determining the purity of oils, each oil combining with a different and known proportion of iodine.

It also forms an extremely powerful and unstable explosive with ammonia water, NHI_2 , particularly when iodine is in slight excess. This is not explosive when wet, but explodes violently when thoroughly dried, upon a touch as light as that of a feather. It is liable to be formed in the "decolorizing" of tincture of iodine with ammonia water.

Among the reducing agents, the most powerful and common are:

Phosphorus and the Hypophosphites.—The first ignites spontaneously in the air, and with greater promptness in contact with

oxidizing agents. Precautions to be observed in weighing and handling it have already been alluded to. The hypophosphites are unstable bodies, becoming oxidized to phosphites or phosphates.

They have been known to explode from trituration. A very low heat decomposes them, liberating the spontaneously combustible phosphoretted hydrogen. They should never be triturated with chlorates or other oxidizing agents.

Sulphur and sulphides combine very readily with oxygen and require special care in mixing and keeping.

Explosions have followed their admixture with chlorates, nitrates and chlorinated lime.

Glycerin is particularly liable to be prescribed with oxidizing agents, and is oxidized by nearly all of them.

COLOR CHANGES.—Changes in the color of galenical preparations are very familiar to the pharmacist. Many tinctures and fluid extracts darken upon standing, particularly when fresh, and a similar change in mixtures is not infrequent. These changes in color are not easy to explain, being, as a rule, imperfectly understood.

From a therapeutic point of view they are commonly unimportant, since no decided change in medicinal properties is observed, but chemically they are interesting, and in a few cases the changes are so marked that the pharmacist should be familiar with them to correctly interpret the appearance of a mixture. Changes in color usually indicate chemical changes in the mixture or liquid, and these may be important, or may not. Thus the iron mixture, page 57, when fresh, is a handsome ruby color, but it gradually darkens to a very deep brown, and then slowly loses its color, becoming at last nearly white. Its taste also changes, being at first sharply astringent, and at last scarcely at all so, showing the reduction of the ferric chloride to the ferrous condition.

In mixtures the changes are most frequently due to the influence of the body upon another, or to a chemical reaction. In only a few instances are these changes considered objectionable, except that the mixtures are rendered less inviting. Preparations containing tannins are a frequent source of trouble from this cause, and cinchona preparations are frequently deprived of their tannin in order to render them miscible with iron salts without forming an ink.

Color reactions are very frequent in chemical analysis, due to the production of a colored salt which may be soluble or insoluble. A complete list of such reactions or of color changes would be impossible in a work of this nature, and in the list below only those which are frequent or important are referred to. A list of liquids which change markedly is also included.

Acetanilid slowly develops a yellow or red color with spirit of ethyl nitrite. This reaction is considered unobjectionable, unless the mixture is allowed to stand too long (two weeks or more), when decomposition products result.

Acid, Benzoic, produces a flesh color with ferric salts.

Acid, Gallic, darkens in contact with alkalis, becoming green to brown with the hydrates or carbonates, and blue with lime water. It gives a bluish-black color with ferric chloride.

Acid, Hydrocyanic, decomposes in the light and air, becoming brown and finally black. This is partly prevented by a little hydrochloric acid or glycerin.

Acid, Nitric, reduces in the light and becomes yellow or brown, due to presence of lower oxides of nitrogen (hyponitric acid, etc.).

Acid, Oleic, and preparations containing it in a free condition, darken and become rancid.

Acid, Salicylic, produces a violet color with ferric chloride, and a red with nitric or nitrous acid. Salts of salicylic acid darken in the presence of the slightest trace of alkali, and are usually slightly acid to avoid this.

Acid, Tannic, in aqueous solution, darkens and the process is hastened by alkalis. Iron salts produce a blue-black, or green-black.

Alcohol usually contains traces of aldehyde or other impurities which cause it to darken in the presence of alkalis. This is one of the causes of change in spirit and aromatic spirit of ammonia.

Aloin.—Some varieties give a greenish-black color with ferric chloride.

Antipyrin quickly produces a green color with spirit of nitrous ether. This was formerly thought to be a poisonous product, but is now considered safe if the mixture is all used up within two weeks. Long standing results in the formation of other and more objectionable bodies.

Bismuth subnitrate forms a red iodo-compound with iodine, and a red nitroso-salicylate with salicylic acid.

Bromoform turns yellow in the light, showing a decomposition which unfits it for use.

Copper salts give a very deep-blue color with excess of ammonia.

Creosote produces a violet color with ferric chloride, which quickly fades to brown.

Cresol and **Phenol** turn red or brown on exposure to light and air, a change which does not detract from their medicinal value, though it does from their appearance.

Iron salts are productive of a variety of colors. Ferrous salts are green, but turn red or brown on oxidation. Ferric salts are brown or red, but lose their color on reduction. The ferric salts, particularly ferric chloride, produce a violet color with phenol, salicylic acid and salicylates, creosote, salol, oil of clove, oil of wintergreen, oil of pimenta, oil of bay, and many bodies containing phenol radicals, as anilin, salol, resorcin, guaiacol, cresols, thymol, etc. Most of these color-reactions are prevented by alkali citrates.

A red color results with acetates, sulphocyanides, antipyrin, phenacetin and mucilage of acacia.

A flesh-color with benzoic acid and benzoates.

A blue or green with thallin, guaiacol, aloin, podophyllin, preparations of guaiac, amidopyrine, anthrarobin, betanaphthol, epinephrin, resorcinol and thymol.

A blue-black with gallic acid, and

A black with tannic acid and preparations containing it, and with gentian.

Tincture of iron chloride forms with phosphoric acid the colorless ferric phosphate, soluble in acids.

Oils of clove, bay and pimenta contain phenol-like principles, which give a violet color with ferric chloride.

Phenacetin, unless perfectly pure, gives pink to red colors with oxidizing agents, such as chlorine water, solution of chlorinated soda, etc. The color is due to the presence of paraphenetidin or its formation in the liquid.

Pyrogallol in solution darkens rapidly.

Quinine Sulphate exhibits a blue fluorescence when dissolved in a very dilute sulphuric acid. This is characteristic of quinine (and quinidine), and is generally expected in quinine solutions. The fluorescence is destroyed by phenacetin and by hydrochloric acid.

Resorcinol turns pink, yellow or deep brown on exposure to light and moisture, more readily in presence of traces of alkaline substances, as ammonia (in the air), alkalis (in glass), etc. With oxidizing agents a series of colorations are produced: thus, ammoniacal silver solution, black; chlorinated soda, violet, finally brown; nitrous acid and spirit of nitrous ether, brown.

Silver salts darken rapidly on exposure to the light. Solutions of silver nitrate, etc., should always be dispensed in amber bottles, or in bottles covered with dark paper, to exclude the light. Blue glass does not prevent this change.

Spirit of Ethyl Nitrite darkens with tannic acid, and produces a yellow or red color with acetanilid and resorcinol, and a bright green with antipyrin, phenazone and thymol.

Syrup of Garlic turns dark in the light, becoming at last almost black.

Syrup of Hydriodic Acid is reduced by light, as shown by the production of a yellow or brown color. It is then unfit for use if it shows the presence of free iodine. A pale straw-color is sometimes observed in the syrup when there is no free iodine present. The cause of this is a conversion of the sugar under the combined influences of the acid and warmth.

If no free iodine can be detected by the starch test (production of a blue color), the syrup may be used.

INCOMPATIBILITIES

A.—Therapeutical

1

R. Hydrarg. chlorid corros. . . . gr. xij
Sacchari. ʒ ss
M. Ft. chart. vi no. Sig.—One at night.

An over-dose of corrosive sublimate. Calomel was wanted instead.

2

R. Acidi arsenosi. ʒ ij
Quininæ sulph. ʒ ss
Syr. sarsap. comp. ʒ iv
M. Sig.—Teaspoonful three times daily.

An over-dose of arsenous acid. Solution of arsenous acid was wanted instead of the pure acid.

3

R. Tincture of nux vomica. . . . Oj
Sig.—Teaspoonful four times daily.

The quantity ordered as well as the dose awaken a suspicion of its use—for a horse, in which case it is safe.

- 4
 R. Liq. plumbi acet. 3 iv
 Sig.—Teaspoonful, as directed. Solution of ammonium acetate (spirit of Mindererus) was intended.
- 5
 R. Morphinae sulphat. 3 j
 Quininae sulphat. gr. j
 M. Ft. pil. xii. The quantities should be transposed or an over-dose of morphine will be given.
- 6
 R. Liq. potassi cit. 3 iv
 Spt. ætheris nitros. 3 j
 Syrupi. 3 j
 Tinct. aconiti. 3 j
 M. Sig.—3ss. t. i. d. Contains an over-dose of tincture of aconite.
- 7
 R. Aconitinae. 0.03
 Sacchari. 4.0
 M. Ft. pulv. vj. Sig.—One every hour. An over-dose of aconitine. Probably 0.003 Gm. was intended instead of 0.03 Gm.
- 8
 R. Ferri sulphat. 3 j
 Strychninae sulph. gr. v
 Acid arsenosi. gr. x
 Quininae sulph. 3 ss
 M. Ft. pil. xxx. Sig.—One at night. The doses of strychnine and arsenic are questionable but not necessarily dangerous, when given only once a day.
- 9
 R. Sodii salicylatis. 3 ij
 Hydrarg. chlorid mitis. gr. xii
 M. Ft. pulv. xij no.
 Sig.—One every 3 hours. The sodium salicylate increases the salivating power of the calomel, and the dose of the latter, considering the frequency of administration, is questionable, though not necessarily dangerous.

B.—Pharmaceutical

- 10
 R. Potassii citratis. 3 j
 Sp. ætheris nitrosi. 3 iv
 Syr. tolu,
 Aquæ. aa 3 j
 M. The dense solution of potassium citrate formed in this mixture is immiscible with alcoholic liquids, and the spirit of nitrous ether separates and floats upon the dense fluid.
- 11
 R. Tinct. cardamomi. 3 j
 Spiritus chloroformi. 3 j
 Codeini. gr. iv
 Pepsini. 3 ss
 M. Sig.—Shake. 3j quat. in die. The pepsin is coagulated by the alcoholic liquids into a rubber-like mass which cannot be diffused through the liquid. Water is needed in such to make an eligible mixture. Two ounces might be added and the dose doubled.
- 12
 R. Quininae sulph. 3 j
 Tinct. nucis vomic. 3 ss
 Spiritus ammoniæ arom. 3 ij
 Syrupi aurantii. 3 vj
 Aquæ. ad. 3 vj
 M. The quinine and oils in the aromatic spirit gradually separate and stick obstinately to the sides of the bottle. The addition of 3iv of mucilage of acacia will emulsify these and make a diffusible mixture.
- 13
 R. Hydrarg. bichlor. gr. j
 Potass. iodidi,
 Ferri et ammon. cit. aa 3 iij
 Tinct. cinchon. comp. 3 iss
 M. Sig.—Sumat drachmam ter in die. Water must be used to dissolve the salts.

R.	Potassii iodidi.....	3 ij
	Quininæ sulphat.....	3 ss
	Syrupi.....	3 j
M.	Aquæ.....ad.	3 iv

23

If compounded as written the quinine iodide formed will coagulate into lumps and cannot be well diffused. A better mixture is obtained by dissolving the potassium iodide in two drachms of water, then add sufficient syrup, in which the quinine is just diffused, to make four fluidounces.

R.	Collodii flexilis, Tinct. iodi, Aquæ ammon.....	āā 3 ij
----	---	---------

24

Collodion is incompatible with aqueous fluids. Spirit of ammonia should be used in place of the water. (See No. 113.)

R.	Chloroformi, Chloralis.....	āā 3 j
	Camphoræ, Ætheris.....	āā 3 ss
	Mentholi.....	3 j
	Alcohol.....	3 vi
	Morphinæ sulphat.....	gr. x
M.	Sig.—“Pain paint.”	

25

Triturate the chloral, camphor, menthol and morphine together until partially liquefied, then rinse mortar with the mixed liquids and shake together until dissolved. A clear liquid (about 4 fl. oz.) results, which becomes cloudy in about half an hour, and in the course of three or four hours flocculent particles of morphine sulphate separate and float upon the surface.

R.	Quininæ sulphatis.....	3 ij
	Strychninæ sulphatis.....	gr. ss
	Acidi phosphorici, diluti, Tinct. ferri chloridi.....	āā 3 ss
	Vini pepsini.....ad.	3 iv
M.	Ft. solutio.	

26

Dissolve the quinine sulphate in the phosphoric acid and mix with the tincture of iron. (This makes a clear solution, but on diluting it both quinine and iron phosphates are precipitated, and the presence of more free acid is needed, in proportion to the amount of dilution, to keep them in solution.) Add ten drops of hydrochloric acid, and to this mixture slowly add the wine in which the strychnine has been dissolved.

If a precipitate occurs which does not redissolve in ten minutes, a few more drops of hydrochloric acid should be added.

R.	Olei morrhue, Tinct. gentianæ comp., Syrupi pruni virgin, Mucilaginis acaciæ.....	āā 3 j
M.	Sig.—A teaspoonful 3 times a day. Mix in inverse order as written.	

27

This cannot be made into an emulsion, and none was expected by the physician. It soon separates, in whatever way it may be mixed, and should be dispensed with a shake-label. The only precaution to be observed in compounding is to avoid adding the tincture directly to the mucilage.

R.	Ichthyolis.....	3 j
	Potassii iodidi.....	3 j
	Glycerini.....	3 j
	Aquæ.....	3 iv
M.		

28

The ichthyol will be partially thrown out of solution by the iodide.

R.	Iodi.....	3 j
	Spiritus camphoræ.....	3 iv
	Aquæ ammoniæ.....	3 iv
	Acidi carbolic.....	3 ss
M.	Ft. solut.	

29

If the iodine be entirely dissolved in the spirit of camphor and the carbolic acid, and then the ammonia water added very slowly, a clear mixture results.

- 30
- R. Copaibæ..... 3 ij
 Spir. ætheris nitros..... 3 iv
 Spir. chloroformi..... 3 j
 Tinct. ferri chlorid..... 3 ij
 Tinct. opii..... 3 j
 Mucil. acaciæ..... 3 ij
- M.
- The spirits and the tinctures are all incompatible with the mucilage, and with any emulsion which may be formed with the copaiba and the mucilage. On mixing the first five ingredients of the prescription in the order written, then adding the mucilage all at once and shaking vigorously, a stringy semi-solid mass is obtained. If the bottle, loosely stoppered, be placed in hot water for a short time, the spirit of nitrous ether will be quickly decomposed and an acid mixture formed which overcomes the other incompatibilities and yields a thin and smooth chocolate-colored emulsion. This continues to effervesce slowly for some time and the bottle must be loosely stoppered.
- 31
- R. Ext. cascariæ fld.,
 Ext. hydrastis fld..... aa 3 ss
 Glycerini..... 3 j
 Aquæ menth. pip..... 3 ij
- M. Sig.—3j post edente.
- The glycerin prevents precipitation of fluid extracts.
- 32
- R. Euphorini..... gr. xvij
 Antipyrini..... 3 ss
- M. Ft. pulv. vj no.
- On triturating these together a thin paste results (which is solidified by addition of water). By first triturating the euphorin with 3j of sugar, then adding the antipyrin and mixing, a dry powder results, which may be dispensed in papers.
- 33
- R. Betanaphthol..... 3 iv
 Sulphuris..... 3 ij
 Balsami Peruviani..... 3 j
 Petrolati..... 3 j
- M. Ft. unguent.
- A homogeneous ointment may be made, but it soon separates, owing chiefly to the insolubility of the Peruvian balsam in the petrolatum. Petroxolin makes a better mixture.
- 34
- R. Potassii bromidi..... 3 jss
 Spiritus æth. nit..... 3 vj
 Syrupi..... ad. 3 ij
- M.
- Dissolve the potassium bromide in 3ijss of water, mix with 3xv of syrup, and then add the nitrous ether. If the nitrous ether is added directly to the bromide solution, before diluting with syrup, a milky mixture results, which clears slowly.
- 35
- R. Fldext. gelsem..... 3 jss
 Fldext. cannabis ind..... gtt. xvij
 Antipyrini..... 3 j
 Chloralis hyd..... 3 jss
 Aquæ..... 3 j
- M.
- An oily liquid separates, which subsequently solidifies into a mass of crystals of chloral-antipyrin. With weak solutions this reaction takes place slowly, or not at all. This prescription should not be dispensed.
- 36
- R. Ext. buchu fld..... 3 ij
 Tinct. cubebæ..... 3 ij
 Tinct. guaiaci ammon..... 3 ss
 Aquæ..... 3 ij
- M.
- The resins in the tinctures and fluid extract are precipitated in an unsightly mass. Acacia, tragacanth or honey should be added to such mixtures to suspend the resins.
- (See under emulsions.)

- 37
- R. Zinci oxidi..... ̄ ij
 Linim. calcis..... ̄ ij
 M.
- 38
- R. Tinct. cantharidis..... ̄ j
 Quininæ sulph..... ̄ ij
 Aquæ ammoniæ..... ̄ ij
 Olei olivæ ut ft..... ̄ iv
 M. Sig.—Apply as directed.
- If the zinc oxide be added to the lime liniment, the latter is broken and a lumpy unsatisfactory mixture is obtained. Triturate the zinc oxide with one ounce of lime water, add an ounce of linseed oil and agitate well. A smooth creamy mixture results.
- Mixed in the order written, a smooth and creamy mixture results. The quinine dissolves in the excess of ammonia, and the oil is emulsified by the ammonia aided by the alcohol in the tincture.

C.—Chemical

- 39
- R. Tinct. ferri chloridi..... ̄ iss
 Quininæ sulphatis..... gr. xv
 Potassii chloratis..... ̄ iij
 Sodii hypophosphitis..... ̄ iss
 Aquæ..... ̄ ij
 M.
- 40
- R. Acid nitromuriat. dilut..... ̄ j
 Spirit. ammoniæ arom..... ̄ j
 M. Sig.—Two drops in water every four hours.
- 41
- R. Argenti nitratis..... gr. ij
 Morphinæ sulphat..... gr. j
 M. Ft. pilulæ xij no. Sig.—One every 3 or 4 hours.
- 42
- R. Argenti nitratis..... gr. x
 Cocainæ hydrochlor..... gr. xij
 Aquæ..... ̄ j
 M. Ft. lotio.
- 43
- R. Liq. acidi arsen..... ̄ j
 Acid nitromur dil..... ̄ v
 Pepsinæ in lamellis..... ̄ ss
 Elixir bismuthi, N. F..... ad. ̄ vj
 M. Sig.—Teaspoonful in water before meals.
- 44
- R. Sodii salicylatis..... ̄ ij
 Sodii phosphatis..... ̄ j
 Aquæ..... ad. ̄ viij
 M. Ft. solut.
- This is a generally incompatible prescription, the iron and chlorate are oxidizing agents, hypophosphite is a reducing agent; and the quinine may precipitate as chlorate, or be partially oxidized. The final composition will depend upon the order of mixing and temperature.
- One ingredient neutralizes the other.
- The two ingredients are incompatible. Mix the silver nitrate with 10 grains of kaolin or talc, and mass with hard petrolatum. Work the morphine thoroughly into the mass and divide.
- Silver chloride is precipitated if dispensed as written. This may be prevented and a clear mixture dispensed (in a bottle protected from the light) by using 16 grains of silver nitrate and filtering out the precipitated chloride. The excess of silver is removed in the filtration, and the cocaine will remain in the form of a nitrate.
- The acids will precipitate bismuth from the elixir. The latter is miscible only with neutral or alkaline fluids.
- Hard water will cause a precipitate of alkaline phosphates. Only distilled water should be used.

45
 R. Acid. salicylici..... ʒ ij
 Ferri pyrophosphat..... ʒ ss
 Sodii phosphatis..... ʒ vj
 Aquam q. s..... ad. ʒ iv
 M. Ft. solut.
 Dissolve the sodium phosphate in 3 ounces of water and the salicylic acid in this solution, then add 5 drops of dilute phosphoric acid to prevent precipitation of the iron. Dissolve the iron in half an ounce of water, add to the other, and make up to 4 ounces.

46
 R. Bismuthi subnit..... ʒ ij
 Spir. ammon. arom..... ʒ j
 Tinct. opii..... ʒ ss
 Syrupi..... ʒ ss
 Mist. cretæ..... ʒ jss
 M.
 The bismuth subnitrate is changed to carbonate by the aromatic spirit of ammonia, and carbon dioxide is liberated.

47
 R. Bismuthi et ammon. cit..... ʒ ij
 Sodii hyposulphitis..... ʒ ij
 Tinct. nucis vomic..... ʒ j
 Infus. calumbæ ut ft..... ʒ vi
 M.
 Black oxysulphide of bismuth is slowly formed and precipitated.

48
 R. Potass. bromidi..... ʒ iiij
 Chloralis..... ʒ ij
 Spt. ammon. arom..... ʒ ss
 Syr. zingiberis..... ʒ j
 Aquæ..... ʒ jss
 M.
 The chloral is decomposed by the alkaline spirit of ammonia, chloroform being formed. The bottle should be tightly stoppered and kept in a cool place.

49
 R. Hydrarg. chlorid..... gr. iiij
 Tinct. cinchon. comp..... ʒ vj
 Spir. ammon. arom..... ʒ j
 M.
 Both ambiguous and incompatible. If the first ingredient means corrosive sublimate, ammoniated mercury will be formed. If calomel, black oxide of mercury will be formed.

50
 R. Liq. potassii arsenitis..... ʒ j
 Hydrargyri bichloridi..... gr. j
 Aquæ..... ʒ iv
 M.
 Here is an incompatibility between the alkali in the arsenical solution and the mercury salt.
 The acid solution of arsenous acid (Valangin's solution) should be substituted for the Fowler's solution and the mixture colored with a few drops of the compound tincture of lavender.

51
 R. Liq. hydrarg. et arseni
 iodidi..... m. lxxx
 Hydrargyri bichloridi..... gr. j
 Aquæ..... ʒ ij
 Five grains of potassium iodide should be added to hold the mercury in solution.

52
 R. Potassii bromidi..... gr. x
 Hydrargyri chloridi mitis..... gr. iiij
 M. Ft. pulv. Mitte tales xij.
 On rubbing these together the calomel is reduced to metallic mercury, with formation of a double bromide of mercury and potassium, which is a powerful poison. $2\text{HgCl} + 4\text{KBr} = (\text{HgBr}_2\text{2KBr}) + \text{Hg} + 2\text{KCl}$.
 This should not be dispensed.

53

- R. Hydrarg. perchloridi..... gr. ss Alkaline carbonates precipitate mercuric chloride, but in this case if the mercuric chloride and potassium iodide be dissolved first, and the ammonium carbonate added to this solution, no precipitate occurs.
- Ammon. carbonat,
Potassii iodidi..... āā gr. v
Aquæ..... 3 j
- M.

54

- R. Hydrarg. protoiodidi..... 3 ss The potassium iodide changes the yellow mercurous iodide into red mercuric iodide and free mercury. The red iodide is much more powerful, and in the above would make dangerous doses. This should not be dispensed.
- Potassii iodidi..... 3 ij
Tinct. cardam. comp..... 3 j
Syr. sarsaparillæ comp..... 3 iij
- M. Sig.—3j quatuor in die.

55

- R. Hydrarg. bichlorid..... 3 j Oxychloride of mercury, as a brick-red powder, is precipitated.
- Sodii boratis..... 3 ij
Aquæ..... 3 iv
- M.

56

- R. Hydrarg. bichlorid,
Ammon. chlorid..... āā gr. iij The ammonium chloride prevents the precipitation of mercuric albuminate and the mixture remains clear.
- Albuminis ovi..... 3 jss
Aquæ destillat..... 3 j
- M.

57

- R. Hydrarg. protochlorid.
Iodoformi..... āā 3 ij These react, on standing, to form mercuric chloride and iodide and chloroform. They should be mixed on paper, without pressure.
- M. Ft. pulv. subtilis. Sig.—Dusting powder.

58

- R. Quinina sulphatis..... 3 ss The quinine is precipitated and redissolved by aromatic spirit of ammonia, but the latter precipitates ferric hydrate from the tincture and makes a thick, muddy mass. Tincture of citrochloride of iron might be used to get a clear solution.
- Tinct. ferri chlorid.,
Spt. ammon. arom..... āā 3 ij
Aquæ font..... 3 xx
- M.

59

- R. Ferri et potassii tart..... 4 Dissolve the iron salt in 30 cc. of water, add the syrup and then add the bromide dissolved in the remainder of the water. If both salts are placed in a bottle and the water added, a dense precipitate results. Mixed as above, the precipitate forms gradually and is less dense.
- Potassii bromidi..... 4
Syrupi..... 15
Aquæ..... ad. 60
- M.

60

- R. Tinct. ferri chlorid..... 3 iij Ammonium carbonate precipitates basic ferric carbonate from the tincture. Tincture of ferric citrochloride should be used. Carbon dioxide will be liberated by acid in the syrup of orange.
- Liq. ammon. acetat..... 3 iv
Ammon. carbonat..... 3 ss
Elix. curacao..... 3 j
Syr. aurantii..... 3 jss
Aquæ..... q. s. ut ft. 3 viij
- M.

- 61
 R. Ammon. carbonat. 3 j
 Spir. æth. nit. 3 j
 Tinct. ferri. chlor. 3 ij
 Spir. mindereri. ad. 3 iv
 M. The ammonium carbonate is incompatible both with the tincture of iron and the spirit of nitre. Ferric subcarbonate is precipitated from the first, and the latter is decomposed. Add the tincture to the mixture last.
- 62
 R. Liq. ferri dialysati. 3 j
 Liq. potass. arsenitis. 3 ij
 Aquæ. 3 iij
 M. The first two are incompatible, dialyzed iron being used as an antidote (in some cases) to arsenic poisoning. The alkali in the Fowler's solution also precipitates the iron in a gelatinous mass.
- 63
 R. Ferri et quininæ cit. 3 ij
 Acid. phosph. dil. 3 ij
 Syr. zingiberis. 3 j
 Tr. cardam. comp. 3 iv
 Aquæ. ad. 3 iv
 M. Sig.—Coch. parv. t. i. d. The phosphoric acid precipitates both the iron and quinine, in part. An excess of potassium or ammonium citrate would hold the iron in solution.
- 64
 R. Syr. ferri iodidi. 3 ss
 Potass. iodidi. 3 j
 Aquæ. 3 jss
 M. The slight precipitate of iron due to the alkali in the iodide may be corrected by adding five grains of potassium citrate to the iodide solution before mixing with the syrup of iron. Any trace of ferric iodide will liberate iodine.
- 65
 R. Plumbi acetatis. 0.25
 Tincturæ opii. 2.00
 Aquæ destillatæ. 200.00
 Syrupi. 25.00
 Sig.—"Wash." Dissolve the acetate of lead in all the water and mix the tincture with the syrup, then mix the two solutions. A cloudy mixture results.
- 66
 R. Zinci oxid. 3 iv
 Acidi salicylici. gr. x
 Amyli. 3 ss
 Adipis lanæ hydros.,
 Petrolati. aa 3 ss
 Olei lavandulæ. q. s.
 M. Ft. unguentum. Zinc salicylate slowly forms and the ointment becomes lumpy on standing. Triturate the acid with a part of the zinc oxide and a little water, then incorporate the other ingredients, and the ointment will remain smooth.
- 67
 R. Liq. plumbi subacet. 3 ij
 Tincturæ opii. 3 ss
 M. Sig.—For external use. Tea-spoonful to a cup of cold water. The solution of subacetate of lead will precipitate most of the principles of the opium and leave a nearly colorless liquid.
- 68
 R. Morphinæ sulphatis. gr. j
 Tinct. lavandul. comp. 3 j
 Aquæ. 3 vij
 M. Sig.—5 j every 4 hours. Santalate of morphine separates as a red flocculent precipitate (caused by the santalum, an ingredient of the tincture).
- 69
 R. Hydrarg. chlorid. corros. gr. j
 Potass. iodidi. 3 ss
 Quininæ bisulphat. 3 j
 Syrupi glycyrrhizæ. 3 j
 Aquæ. 3 iij
 M. The alkaloid is precipitated by the double iodide of mercury and potassium.

- 70
 R. Hydrarg. bichlorid. gr. j
 Potassii iodidi. $\frac{3}{4}$ ss
 Tr. cinchon. comp. $\frac{3}{4}$ ij
 M.
 No precipitation—only a slight cloudiness—occurs in this case, because the iodohydrargyrate of the alkaloids (in the tincture) are held in solution by the alcohol in the tincture. Dispense with a shake label.
- 71
 R. Morphinæ sulph. gr. j
 Tr. catechu comp. $\frac{3}{4}$ ij
 Tr. zingiberis. $\frac{3}{4}$ ss
 Syrupi ejusdem. ad. $\frac{3}{4}$ ij
 M.
 Tannate of morphin is precipitated.
- 72
 R. Quininæ sulphatis. $\frac{3}{4}$ ss
 Acid sulphurici dilut. $\frac{3}{4}$ j
 Tinct. cardamomi comp. $\frac{3}{4}$ ij
 Syr. aurantii. $\frac{3}{4}$ vj
 Aquæ. $\frac{3}{4}$ iij
 M.
 The tannin in the tinct. cardamom precipitates a portion of the quinine as tannate, and makes a cloudy mixture. There would be but little loss of quinine if this were filtered out.
- 73
 R. Caffeinæ citratæ. gr. xx
 Spt. ammon. arom. $\frac{3}{4}$ ij
 Elix. guaranæ. ad. $\frac{3}{4}$ ij
 M.
 Caffeine forms an exception to the general incompatibility of alkaloids. It is quite soluble in warm water and dilute alcoholic liquids, and does not form salts easily. In the above the citric acid is neutralized by the aromatic spirit, but the mixture remains clear, the caffeine not being precipitated.
- 74
 R. Hydrarg. ioid. rubri. 0.02
 Pilocarpinæ muriatis. 0.05
 Liq. adrenalini chlor. 0.10
 Petrolati albi. 5.00
 M. Ft. ung.
 The mercuric iodide must not be rubbed dry with the pilocarpin, and the adrenalin solution will darken if a steel spatula be used. The three active substances should be incorporated separately with portions of the petrolatum, and then mixed, avoiding the use of a metallic spatula.
- 75
 R. Cocainæ mur. gr. x
 Hydrargyri iodidi rubri. gr. ij
 Petrolati albi. $\frac{3}{4}$ iv
 M. Ft. ung.
 The cocaine muriate should be powdered finely and mixed with a portion of the petrolatum, and the mercuric iodide treated with another portion. Cocaine will reduce the mercury salt if rubbed directly with it.
- 76
 R. Ferri et quininæ citratis. $\frac{3}{4}$ ij
 Potassii citratis. $\frac{3}{4}$ ij
 Acidi citrici. $\frac{3}{4}$ j
 Aquæ. ad. $\frac{3}{4}$ vj
 M. Ft. solut.
 Acid citrate of quinine separates in crystals after standing a few hours. The addition of a small quantity of ammonium chloride was recommended to prevent this.
- 77
 R. Potassii iodidi,
 Ferri et quin. cit. aa $\frac{3}{4}$ ij
 Syrupi. $\frac{3}{4}$ j
 Aquæ. $\frac{3}{4}$ iij
 M.
 Quinine iodide is precipitated in a bulky mass. Can be diffused by shaking, but more syrup will make a better mixture.

78

- R. Quininæ bisulphatis..... 5 ss Quinine acetate is precipitated and
 Liq. ferri et ammon. acet... 5 ij the liquor is partially decolorized.
 M.

79

- R. Quininæ sulphatis..... 1.0 Nitric acid liberates iodine from
 Acidi nitrici dilut..... 1.0 potassium iodide, and the quinine is
 Potass. iodid..... 2.0 precipitated. Should not be dispensed,
 Aquæ..... 100.0 unless for external use.
 M.

80

- R. Tinct. ferri chlorid..... 5 ij On standing a double salt of strych-
 Strychninæ sulph..... gr. j nine and mercury is formed and depos-
 Hydrarg. chlorid corros..... gr. ij ited. If aromatic elixir be used in place
 Acid hydrochloric dil..... 5 ij of syrup of citric acid, the alcohol keeps
 Syrupi acidi citrici ut. ft.... 5 iv this in solution.
 M.

81

- R. Piperazin..... 5 j Piperazin is slightly alkaline and
 Strychninæ sulph..... gr. ss would precipitate some of the strych-
 Syr. aurantii..... 5 j nine but the acid in the syrup prevents
 Aquæ chloroformi..... 5 v this. Dissolve the piperazin in four
 M. ounces of chloroform water and add the
 syrup. Then dissolve the strychnine
 in the rest of the water and mix.

82

- R. Liq. acidi arsenosi..... 5 iv Strychnine arsenite is formed and
 Strychninæ sulphat..... gr. j precipitated. Alcohol in place of the
 Aquæ destillat..... 5 iv water will prevent this precipitation.

83

- R. Iodi..... gr. xx If potassium iodide be used to dis-
 Ext. opii..... gr. x solve the iodine, the alkaloids in the
 Camphoræ..... gr. xv extracts will be rendered insoluble.
 Ext. belladonnæ..... gr. xx Dissolve the iodine and camphor in a
 Adipis benz..... 5 j little ether, and incorporate with half
 M. Ft. unguent. the lard, warming gently and stirring
 until the ether has evaporated. Soften
 the extracts with water, incorporate
 with the remainder of the lard and mix
 with the first.

84

- R. Cocainæ hydrochlor..... gr. viij The cocaine (alkaloid) is precipitated
 Sodii boratis..... 5 j by the borax. By triturating the borax
 Aquæ..... 5 j with a drachm of glycerin before dis-
 M. solving this is prevented. Or boric acid
 may be substituted for the borax.

85

- R. Sodii salicylatis..... 5 ij The sodium salicylate is decomposed
 Aquæ menth. virid..... 5 ss by the acid, salicylic acid being thrown
 Acid sulphurici dilut..... 5 j out of solution.
 M.

86

- R. Sodii salicylat..... 5 ss The spirit of nitrous ether must be
 Spt. ætheris nitros..... 5 ss neutral or it will throw salicylic acid out
 Aquæ..... 5 jss of solution. If acid in reaction, neu-
 M. tralize with sodium or potassium car-
 bonate before adding to the sodium
 salicylate solution, being careful not to
 add too much alkali, as an excess will
 make a dark-colored solution.

- 87
 R. Morphinae sulphatis..... gr. iv
 Acidi tannici..... ʒ ss
 Acidi carbolic..... ʒ ss
 Glycerini,
 Aquæ..... aa ʒ ss
 M. Ft. solut.
- The glycerin prevents precipitation of morphine tannate in this mixture.
- 88
 R. Codeinae..... gr. ij
 Acid phosphorici dilut..... q. s.
 Acid hydrocyanici dilut..... m xx
 Tincturæ iodi..... m x
 Aquam q. s..... ad. ʒ iv
 M. Ft. solut.
- The tincture of iodine precipitates the codeine, but on adding the hydrocyanic acid the precipitate dissolves.
- 89
 R. Acidi nitrohydrochlor..... ʒ ss
 Tinct. cardam. comp..... ʒ jss
 M.
- This is likely to explode after an hour or two.
- 90
 R. Iodi..... 10
 Alcohol..... 30
 Olei terebinth..... 200
 M. Sig.—For inhalation.
- Triturate the iodine with the alcohol, and add this mixture to the turpentine in small portions. An explosion will result if the iodine is added directly, or too suddenly, to the turpentine.
- 91
 R. Acidi chromici,
 Glycerini,
 Alcoholis..... aa p. e. ad. ʒ ss
 M. Sig.—Apply as directed.
- Very inflammable and explosive. Should not be dispensed.
- 92
 R. Bismuthi subnit..... ʒ ij
 Sodii bicarb..... ʒ j
 Aq. menth. virid..... ʒ ij
 M.
- The bismuth and sodium salts react slowly, forming bismuth carbonate and sodium nitrate, with evolution of carbonic acid gas. The bottle should be loosely stoppered.
- 93
 R. Bismuthi subnit..... ʒ ss
 Mist. cretæ..... ʒ jss
 Tr. opii..... ʒ iv
 M.
- The bismuth subnitrate will be slowly decomposed by the chalk in the chalk mixture, carbonic acid gas being evolved.
- 94
 R. Potassii chloratis..... ʒ iiij
 Tinct. ferri chlorid..... ʒ ij
 Glycerini..... ʒ ij
 M. Sig.—Apply with a camel's-hair brush.
- Must be kept cold (below 70° F.) to prevent explosion. Stopper loosely as an additional precaution and caution against a possible combustion.
- 95
 R. Tinct. aconiti..... m. xvj
 Spt. ætheris nitros..... ʒ ss
 Liq. ammon. acet..... ʒ jss
 M.
- The ammonium acetate throws the nitrous ether out of solution, and an effervescence ensues. If the ingredients are warm, the effervescence is very active.
- 96
 R. Spir. ætheris nitros..... ʒ vj
 Ext. buchu fluidi,
 Ext. uvæ ursi fld..... aa ʒ iv
 Syrupi q. s. ut. ft..... ʒ iv
 M.
- A slow reaction between the tannin in the fluid extracts and the spirit of nitre will occur, and the bottle may burst if tightly stoppered. Shake well before delivering, and instruct the customer to keep loosely stoppered.

97

R.	Acidi salicylici.....	℥ v
	Lithii carbonatis.....	gr. x
	Sodii bicarbonatis.....	℥ iij
	Olei gaultheriæ.....	℥ iij
	Glycerini.....	℥ iv

M.

Heat the glycerin to about 50° C., dissolve the salicylic acid in it by trituration, and add the lithium and sodium salts gradually, stirring to favor the disengagement of gas. Then cool, add the oil and dispense with a shake label. Unless the reaction is hastened by heat, the effervescence will be extremely slow.

98

R.	Potassii bitart.....	℥ j
	Potassii iodidi.....	℥ j
	Spir. æth. nitros.....	℥ iv
	Syr. aurantii.....	℥ j
	Aquæ.....ad.	℥ x

M.

This cannot be compounded without reaction between the first three ingredients resulting in the entire decomposition of the spirit of nitrous ether, and partial decomposition of the other two. The "Art of Dispensing" directs to proceed as follows: "If compounded at

all, dissolve ℥j of cream of tartar and 8 grains of potassium iodid in 4 oz. of water, add the spirit of nitrous ether, and stir briskly so that the gas may escape. Allow to stand half an hour, in order to get rid of the nitrous fumes. Then make up the rest of the mixture and add to this. The object of this procedure is to limit the action of the nitrous ether, for while theoretically the 4 drachms will liberate the iodine from about 8 grains only of the iodide, the liberated nitrous oxide on coming in contact with the air is changed to higher oxides, which are capable of decomposing iodide, so that if the mixture were made up at once, iodine would continue to be liberated until the whole of the potassium iodide is decomposed."

99

R.	Ammonii carbonat.....	℥ ij
	Syrupi simplic.,	
	Mucil. acaciæ.....āā	℥ iss
	Aquæ.....	℥ ij

M.

If the mucilage is old an effervescence may ensue, caused by the acid in the mucilage reacting upon the carbonate.

100

R.	Syr. scillæ.....	℥ j
	Syr. senegæ.....	℥ ss
	Potass. bicarb.....	℥ ij
	Tinct. opii.....	℥ ij
	Syrupi.....ad.	℥ iv

M.

The syrup of squill contains acetic acid, which neutralizes the ammonia in the syrup of senega, and causes an effervescence with carbonates. The bicarbonate should be added first, and when the effervescence has ceased, the other ingredients are added.

101

R.	Ammonii carbonat.....	℥ j
	Ammonii chloridi.....	℥ ss
	Syrupi scillæ.....	℥ j
	Syrupi ipecacuan.....	℥ j
	Syrupi pruni virgin.....	℥ ij

M. Sig.—℥ j for cough.

The acids in the syrups of squill and ipecac react slowly with the ammonium carbonate, liberating carbonic acid gas.

102

R.	Codeinæ.....	gr. iv
	Ammon. chlorid.....	℥ iij
	Ext. hyoscyam. fld.,	
	Tr. nucis vomic.,	
	Sp. chloroformi,	
	Elix. cascar. sagrad.....āā	℥ iv
	Aquæ.....q. s. ut. ft.	℥ vj

M.

The alkali in the elixir of cascara reacts with the ammonium chloride, liberating ammonia gas. Sufficient pressure may be generated, in a warm place, to blow out the stopper of the bottle.

103

- R. Tinct. iodi..... 3 j Compound camphor liniment (Ph.
 Linim. camph. comp..... 3 ii j B.) contains ammonia water, and is
 M. liable to form the explosive nitrogen-
 iodine compound (NHI_2) with the
 tincture of iodide. This compound is
 an extremely powerful explosive, and
 very unstable when dry.

104

- R. Iodol..... 0.5 If the iodol and oxide of mercury be
 Hydrarg. oxid. flav..... 0.2 rubbed together, an explosion will take
 Petrolati..... 10.0 place. This does not occur in presence
 M. Ft. ung. of the petrolatum or a portion of it.

105

- R. Argenti nitratis..... 3 j The silver nitrate is rapidly decom-
 Aquæ rosæ..... 3 j posed by the rose water, the liquid turn-
 M. Ft. lotio. ing black and depositing a heavy sedi-
 ment. Distilled water should be used
 and the solution dispensed in an amber
 or colored bottle, to prevent reduction
 of the silver salt by light.

106

- R. Oleatis morphinæ..... 3 ss If fresh and light-colored when dis-
 M. Sig.—Apply as directed. posed, this rapidly darkens.
 The same change in color occurs with
 mercury oleate.

107

- R. Potassii permanganatis..... 3 j The glycerin decomposes the perman-
 Glycerini..... 3 j ganate, entirely discharging the color
 Aquæ..... 3 ij of the solution and forming a dense
 M. brownish precipitate.
 If the permanganate is added directly
 to the glycerin, the latter is liable to
 inflame.

108

- R. Bismuthi subnit..... 3 ij The insoluble bismuth salt gradually
 Sodii salicylat..... 3 ij turns red, owing to the formation of
 Aquæ cinnamomi..... 3 ij bismuth nitro-salicylate.

109

- R. Bismuthi subnit..... 3 ij Red iodide of bismuth is formed in
 Pulv. tragacanth..... q. s. this mixture. The bismuth should be
 Tinct. nucis vomicæ..... 3 ij given separately as a powder.
 Potassii iodidi..... 3 ij
 Spiritus chloroformi..... 3 ii j
 Aquæ..... q. s. ut. ft. 3 xi j
 M.

110

- R. Tinct. ferri chlorid..... 3 ij Makes an inky mixture. The addi-
 Tinct. gentianæ comp. . . . ad. 3 iv tion of 30 grs. potass. citrate will pre-
 M. Sig.—Teaspoonful after meals. vent this.

111

- R. Tinct. ferri chlorid..... 3 j The quinine is soluble in the tinctures,
 Quininæ sulph..... 3 j but the mixture is inky.
 Tinct. cinchon. comp..... 3 ij
 M. Sig.—3 j in aq. t. i. d.

- 112
- R. Tinct. ferri chloridi..... ʒ ij The tannin extracted from the orange
Syr. aurantii corticis..... ʒ j peel may make a dark mixture with the
Aquæ..... q. s. ad. ʒ iv tincture of iron.
- M.
- 113
- R. Tinct. iodi,
Aquæ ammoniæ,
Collodii..... aa ʒ j Pyroxylin is first precipitated by the
water of ammonia, but after about 24
hours is partially reduced by the excess
of ammonia and redissolved. The
mixture is nearly colorless at first, but
turns reddish-brown on standing.
With spirit of ammonia the mixture
remains clear from the first, but under-
goes similar color-changes. Various
ammonia compounds are formed.
- M.
- 114
- R. Acidi carbolici..... ʒ ss Makes a deep violet-colored mixture.
Tr. ferri chlorid..... ʒ j
Glycerini..... ʒ j
- M. Sig.—Apply with brush every
3 hours.
- 115
- R. Salolis..... ʒ ij Suspend the salol in the glycerin,
Tinct. ferri chlorid..... ʒ ij add the water and then the tincture
Spiritus æth. nit..... ʒ j and spirit. A lighter-colored and less
Glycerini..... ʒ ss changeable mixture is obtained in this
Aquæ..... ʒ v way than if the salol be dissolved in the
tincture and spirit.
- M.
- 116
- R. Tinct. ferri chlorid..... ʒ ss Very dark blue at first, but the color
Acidi carbolici..... ʒ j becomes discharged after a short time.
Acidi sulphuros..... ʒ iiij
Aquæ..... ad. ʒ viij
- M. Ft. garg.
- 117
- R. Tinct. ferri chloridi..... 2 The first two are incompatible, insol-
Acidi phosphorici dil..... 2 ule phosphate of iron being formed
Syrupi..... 60 which is soluble in an excess of phos-
phoric or hydrochloric acid, making a
colorless solution.
- M.
- 118
- R. Liq. potassii arsenitis..... ʒ ijss The first and second and third are
Tinct. ferri chloridi,
Acidi phosphorici dilut... aa ʒ j incompatible, but a clear, colorless solu-
tion is obtained by first mixing the
Fowler's solution and phosphoric acid,
then adding the tincture of iron and
lastly the water. "Shake."
- M.
- 119
- R. Tinct. ferri chloridi..... ʒ ij A very dark mixture results, and a
Quininæ sulphat..... gr. xvijj precipitate may form on standing,
Spt. chloroformi..... ʒ j owing to a reaction between the iron
Aquæ caryophylli... ad. ʒ vi and eugenol in the clove.
- M.
- 120
- R. Antipyrini..... ʒ j A green color is developed on mixing
Sp. ætheris dulc..... ʒ ijss the antipyrin with the spirit of nitrous
Syr. limonis..... ʒ ss ether, due to the formation of isonitro-
soantipyrin. It may be dispensed.
- M.

121

- R. Potassii iodidi..... ʒ jss The official compound spirit of ether usually contains some free acid, which may liberate iodine from the potassium iodide and color the mixture.
 Spiritus ætheris comp.,
 Syrupi,
 Aquæ.....aa ʒ j

M.

122

- R. Tr. ferri chlor..... ʒ jss Iodine is liberated from the potassium iodide by the iron and acid, and this, with the undecomposed iodide, precipitates the quinine, making a very unsightly and unpleasant mixture.
 Acidi nitromur. dil..... ʒ jss
 Quininae muriat..... gr. x
 Potassii iodidi..... ʒ ss
 Ext. digitalis fld..... ℥ x
 Syrupi simplic.....ad ʒ ij The iodide should not be included in such a mixture.

M.

123

- R. Liq. iodi comp., The iodine will be partly converted into colorless iodide and iodate of potassium.
 Liq. potassæ.....aa ʒ j

M.

124

- R. Acidi tannici..... 1.0 The tincture of iodine will be decolorized by the tannin.
 Tinct. iodi..... 0.5
 Glycerini..... 10.0
 Aquæ..... 50.0

M.

125

- R. Potassii chloratis..... ℥ ij If the syrup of iodide of iron contains any free acid (citric or hypophosphorous acids put in to preserve it), or if it has oxidized, a reaction is likely to ensue, liberating chlorine from the chlorate, which in turn liberates iodine from the iodide, and the mixture becomes brown, then deposits iodine. This reaction can be only prevented by keeping the solution neutral by addition of a little calcium carbonate or similar neutralizing body.
 Syr. ferri iodid..... ʒ iv
 Spiritus chloroformi..... ℥ xx
 Syrupi..... ʒ iv
 Aquæ.....ad. ʒ ij

M.

126

- R. Sodii salicylat..... gr. x Becomes red in a few hours.
 Ammon. carbonat..... gr. iij
 Spt. ætheris nit..... ℥ xx
 Spt. chloroformi..... ℥ x
 Aquæ.....ad. ʒ j

M.

127

- R. Ferri sulphat..... gr. viii Becomes dark colored owing to formation of nitrosyl ferrous sulphate from interaction of iron sulphate, sulphuric acid and nitrous ether.
 Quininae sulphat..... gr. viii
 Acid sulphur. dil..... ʒ ii
 Spir. æth. nitros..... ʒ iss
 Aquæ.....ad. ʒ viii

M.

128

- R. Tinct. ferri chlor..... ʒ iv The iron chloride liberates iodine from potassium iodide and the strychnine is entirely precipitated.
 Potass. iodid..... ʒ i
 Liq. ammon acet..... ʒ iv
 Strychninae sulph..... gr. ss
 Glycerini..... ʒ ss
 Aquæ.....ad. ʒ vi

M.

129

R.	Sodii salicylat,		
	Sodii bicarbonat,		
	Sodii borat.....aa	5	i
	Phenol liquificat.....	m	xx
	Ol. cassiæ.....	gtt.	iv
	Aquæ dest.....	5	x

M. Sig.—A dessertspoonful as directed.

Darkening in this mixture can be prevented by rubbing the borax with 5 ii glycerin before adding to the other ingredients, but this will make an acid mixture, will decompose the bicarbonate, and will probably nullify the doctor's desire.

130

R.	Phenylis salicylatis.....	5	i
	Spiritus ætheris nitrosi.....	5	iv
	Tinct. ferri chloridi.....	5	iv
	Glycerini.....	5	i
	Syrupi.....	5	i
	Aquæ.....ad.	5	vi

M. Sig.—A tablespoonful every 3 hours.

If the salol be dissolved in the spirit of nitrous ether and added to the tincture a dark violet solution is obtained. If, however, the salol be first suspended in the glycerin and syrup, then the other ingredients added, the mixture will be almost colorless.

131

R.	Sodii nitritis.....	3.0
	Potass. iodid.....	8.0
	Spir. æth. nitros.....	12.0
	Spir. lavand co.....	60.0
	Aquæ.....	120.0

M. Sig.—8 every 6 hours.

The spirit of nitrous ether will liberate iodine from the potass. iodide on standing. The two should not be dispensed together.

132

R.	Potass iodidi.....	4.0
	Sodii salicylat.....	15.0
	Syr. aurantii.....ad.	120.0

M. Sig.—Teaspoonful as directed.

The acid in syrup of orange will liberate salicylic acid. A neutral medium, as elixir of orange or simple syrup with tincture of orange should be used.

133

R.	Potassii iodidi.....	5	ii
	Bismuthi subnit.....	5	iii
	Strychninæ sulph.....	gr.	i
	Syrupi.....	5	ss
	Aquæ.....ad.	5	iv

M. Sig.—A teaspoonful three times a day after meals.

The potassium iodide will precipitate the strychnine and also form red iodide of bismuth by reaction with the subnitrate. The physician should be consulted.

134

R.	Mentholis.....	1.0
	Resorcinolis.....	1.0
	Spir. ætheris nitros.....	25.0
	Alcohol.....	50.0
	Aquæ menth pip.....	50.0

M. Ft. sol. Sig.—For external use. Apply as directed.

The nitrous ether reacts with the resorcin forming a green dye which stains badly and also precipitates in the mixture.

135

R.	Hydrarg. chlorid mit....	gr.	vi
	Ext. hyoscyani.....	gr.	ii
	Phenylis salicylatis.....	gr.	v
	Acetphenetidini.....	gr.	xxiv
	Sodii bromidi.....	gr.	xxx

M. Ft. capsul. no. vi.
Sig.—One every 2 hours for 3 doses.

Sodium bromide is incompatible with calomel and in this case would cause a toxic dose. Should not be dispensed.

136

- R. Magnesii sulphatis..... 4.0 Very bulky, almost gelatinous basic
 Ferri sulphatis..... 0.6 quinine acetate separates after two or
 Quininæ sulphatis..... 1.0 three minutes. More acid makes it
 Potassii acetatis..... 8.0 worse, unless an excessive amount is
 Acidi sulphuric arom..... q. s. used. Precipitation can be avoided by
 Syrupi aurantii..... 30.0 using 90 cc. of glycerin in place of an
 Aquæ..... ad. 180.0 equal amount of water.

M.

137

- R. Potass iodidi..... 3 i There is acid enough in the tincture
 Sodii nitritis..... gr. xx to liberate nitrous acid from the nitrite,
 Tr. gentianæ co..... 3 ii and this in turn liberates iodine from
 Syrupi..... 3 iv the iodide. The mixture must be
 Aquæ menth pip..... ad. 3 vi made neutral to avoid this.

M.

138

- R. Cocainæ hydrochlor.... gr. viii The bismuth subnitrate will slowly
 Cerii oxalatis..... gr. cccxx react with the bicarbonate, liberating
 Bismuthi subnit..... 3 i carbon dioxide. Cocaine will also be
 Sodii bicarbonatis..... 3 iv precipitated in a form not easily
 Aquæ..... ad. 3 iv diffused.

M.

139

- R. Hydrarg. chlorid corros.... gr. i Mercuric chloride is reduced to mer-
 Liq. potassii arsenit..... 3 ii curous chloride by the arsenite. This
 Syrupi..... 3 i can be hindered by a slight excess of
 Aquæ..... ad. 3 iii hydrochloric, or by one ounce of gly-
 erin. Solution of sodium arsenate
 would be better in this combination.

M.

140

- R. Liq. epinephrini..... 3.00 Epinephrine is decomposed by borax.
 Sodii boratis..... 0.50 Chloretone is not all soluble in the salt
 Chloretoni..... 0.60 solution.
 Liq. sodii chlorid physiol... 30.00

M. Ft. sol.

141

- R. Argpyrol..... gr. xv The iodine decomposes the argyrol
 Potassii iodidi..... gr. xx and the mixture gradually becomes
 Iodi..... gr. xx irritating.
 Glycerini..... ℥ xv
 Aquæ..... ad. 3 i

M.

142

- R. Magma magnesiae..... 3 ss Turns black on long standing, due to
 Magma bismuthi..... 3 ss the reduction of the bismuth by
 Elixii lactated pepsin.... ad. 3 vi inverted sugar in the elixir. Will
 blacken at once if heated.

M.

143

- R. Apothesine..... gr. iv Precipitates apothesine base. Use
 Sodii boratis..... gr. x $\frac{1}{2}$ drachm of glycerin with the borax.
 Acidi borici..... gr. x
 Aquæ destillat..... 3 ii

M. Ft. sol.

144

- R. Sodii bicarbonatis..... gr. xv Forms (caustic) sodium hydroxide
 Magnesii oxidi..... gr. x slowly on standing.
 Tinct belladonnæ..... ℥ v
 Aquæ. menth. pip..... ad. 3 i

M.

- 145
- R. Bismuthi subsalicylatis..... ʒ ii Effervesces slowly, due to the slow
Sodii bicarbonatis..... ʒ iv liberation of salicylic acid by action of
Cerii oxalatis..... ʒ ss water in the elixir upon the subsalicyl-
Elixi aromaticir.....ad. ʒ iii ate.
- M.
- 146
- R. Spir aether nit..... ʒ i The acids in the syrups and spirit will
Sodii nitritis..... ʒ i liberate nitrous acid from sodium nitrite.
Aceti scillæ..... ʒ vi The acids should be neutralized before
Syr. scillæ..... ʒ vi adding the nitrite.
Syr. tolut..... ʒ vi
Aquæ.....ad. ʒ viii
- M.
- 147
- R. Sodii nitritis..... gr. xv Acid in the syrup liberates nitrous
Tr. strophanthi..... ʒ i acid. The syrup should be neutralized.
Syr. hypophos co..... ʒ ii
Aquæ.....ad. ʒ viii
- M.
- 148
- R. Zinc permanganat..... ʒ i The zinc permanganate acts upon
Fldext. hydrastis..... ʒ iiss the fluidextract of hydrastis with almost
Aquæ dest..... ʒ iii explosive violence.
- M.
- 149
- R. Auri chlorid..... gr. i The gold chloride is reduced and a
Plumbi acetatis..... gr. x deep purplish fluid is formed.
Aluminis..... gr. xii
Creosoti..... ʒ vi
Sodii boratis..... ʒ iv
Glycerini..... ʒ iv
- M.
- 150
- R. Tinct iodi..... ʒ i The iodine reacts with the hydro-
Acid hydrocyan. dil..... ʒ i cyanic acid forming hydriodic acid and
Syr. tolutan..... ʒ i liberating cyanogen. A colorless mix-
Aquæ.....ad. ʒ vi ture is thus obtained.
- M.
- 151
- R. Potass iodid..... ʒ ii A yellow solution (or perhaps a pre-
Ammon bromid..... ʒ iii cipitate) is formed from the iodide and
Elix bismuth et pepsin ad. ʒ iv bismuth. The bromide causes a slow
darkening in a strong light,—much
more rapidly if the elixir is alkaline.
Placing in the dark prevents this—or
even restores the light color.
- M.
- 152
- R. Potass bromid..... gr. xv Turns black on exposure to light, and
Liq. bismuth et ammon cit. ʒ i becomes white again on being stored in
Sodii bicarb..... gr. xv the dark.
Ol. menth. pip..... ʒ i
Aq. chloroformi.....ad. ʒ iv
- M.
- 153
- R. Hydrarg. chlorid mit..... gr. vi In a flask there was found to be no
Podophyllin..... gr. ss appreciable oxidation of the calomel
Potass chloratis..... ʒ i by the chlorate in 0.3 per cent hydro-
chloric acid at body temperature for an
hour, but a slight oxidation occurred
within two hours and this action con-
tinued for several hours after.
- M. Ft chart no. vi
Sig.—One every hour. Four
hours after last dose take a dose of
salts or oil.

- 154
- R. Hydrarg. chlorid corros... gr. xxx
Tinct. sapon mollis..... $\frac{3}{4}$ iv
M. Ft. sol.
- Insoluble mercuric oleate would be formed, but if the mercuric chloride be dissolved in two drachms of alcohol, then a drachm of potassium iodide dissolved in 40 minims of water be added to it, this mixture will form a clear solution with the tincture.
- 155
- R. Olei rusci..... $\frac{3}{4}$ vi
Acid salicylici..... $\frac{3}{4}$ iii
Sapon. viridis..... $\frac{3}{4}$ iss
Petrolati.....ad. $\frac{3}{4}$ iv
M. Ft. mg.
- Powder the salicylic acid finely, mix with the oil, then with the petrolatum, and lastly add the soap. Acid and soap are incompatible, but the reaction is prevented by this method of mixing.
- 156
- R. Betanaphtholis..... $\frac{3}{4}$ i
Phenolis..... gr. xv
Balsami peruv..... $\frac{3}{4}$ iv
Ung. sulphuris..... $\frac{3}{4}$ i
M.
- Will not mix smoothly. Use 72 grains of sulphur and 408 grains of solid petroxolin for the sulphur ointment, and a smooth ointment will result.
- 157
- R. Bals. tolu..... $\frac{3}{4}$ ii
Creosoti..... $\frac{3}{4}$ i
Ung. sulphuris..... $\frac{3}{4}$ i
M. Ft. ung.
- Dissolve the tolu in about half an ounce of ether and filter through a pellet of cotton into the sulphur ointment, previously melted. Continue the heat, with stirring until the ether is evaporated, then add the creosote, remove from the heat, and stir until it congeals.

Prescriptions from State Board Examinations

FOR CRITICISM, SUITABILITY FOR COMPOUNDING, METHODS OF MIXING, TRANSLATION INTO OTHER METROLOGICAL SYSTEMS, AND PRACTISE

- | | |
|---|---|
| <p>I</p> <p>R. Morphinae sulph..... gr. xii
Acidi borici.....
Sodii boratis.....āā gr. v
Aq. destill..... $\frac{3}{4}$ i
Misce. Ft. solu. s. a.
Sig.—Drop into eye several times daily.</p> | <p>2</p> <p>R. Plumbi acetatis..... $\frac{3}{4}$ ss
Aluminis..... gr. xv
Aquae rosae..... $\frac{3}{4}$ iv
M. Sig.—Lotion. (Ala.)</p> |
| <p>3</p> <p>R. Ammon carb..... $\frac{3}{4}$ ii
Syr. tolu,
Syr. scillae.....āā $\frac{3}{4}$ ii
M. Sig.—One teaspoonful when necessary, for cough.</p> | <p>4</p> <p>R. Sod. salicylat..... $\frac{3}{4}$ i
Glycerini..... $\frac{3}{4}$ iss
Olei gaulther..... $\frac{3}{4}$ i
Tinct ferri chlor..... $\frac{3}{4}$ iss
Acid citric..... gr. v
Liq. ammon acet.....ad. $\frac{3}{4}$ ii
M. Sig.—One dessertspoonful two or three times a day. (Tex.)</p> |
| <p>5</p> <p>R. Acidi nitromuriat..... $\frac{3}{4}$ ii
Tinct. nucis vom..... $\frac{3}{4}$ i
Tinct. cardam co..... $\frac{3}{4}$ ii
Tinct. gent. co. ad..... $\frac{3}{4}$ iv
M. Sig.—One teaspoonful after meals. (Tex.)</p> | <p>6</p> <p>R. Quininae sulph..... gr. xlviii
Fldext glycyrrhizae..... $\frac{3}{4}$ ss
Acidi sulph. dil..... $\frac{3}{4}$ xxx
Syrapi.....ad. $\frac{3}{4}$ ii
M. Sig.—One teaspoonful every 4 hours. (Tex.)</p> |

7

- R. Liq. potass arsenit..... ʒ iv
 Antipyrini..... ʒ ii
 Tinct. ferri chlorid..... ʒ iv
 Glycerini..... ʒ iv
 Aquæ..... ad. ʒ iii
 M. Sig.—ʒi every 2 hours. (N. Y.)

9

- R. Potass iodid..... ʒ iii
 Bismuth subnit..... ʒ ii
 Ess. pepsini..... ʒ ii
 M. Sig.—Teaspoonful every 2 or 3 hours for bowels. (Fla.)

11

- R. Potass chlorat..... ʒ iii
 Chloral hydrat..... ʒ iss
 Tinct. ferri chlor..... ʒ iii
 Aquæ..... ad. ʒ iii
 M. Sig.—A teaspoonful every 2 hours.
 Gargle then swallow. (New Mex.)

13

- R. Ammon. carb..... ʒ ss
 Pulv. ipecac..... ʒ ss
 Syr. scillæ..... ʒ i
 Syr. prun. virg..... ʒ ii
 M. Sig.—ʒi omnia 3 hora.
 (New Mex.)

15

- R. Tinct. ferri chlor..... ʒ iv
 Syr. hypophos. co..... ʒ vi
 M. Sig.—ʒi t. i. d. (Mass.)

17

- R. Strych. sulph..... gr. ss
 Kali iodidi..... ʒ iss
 Syr. sarsap. co..... ad. ʒ iv
 M. Sig.—One teaspoonful every 3 or 4 hours as directed. (Vt.)

19

- R. Atropinæ sulph..... gr. i
 Cocainæ mur..... gr. ii
 Sodii boratis..... gr. vi
 Aquæ dest..... ʒ i
 M. Ft. sol. et filtra.
 Sig.—Collyrium. (N. H.)

21

- R. Santonini..... gr. xii
 Hydrarg. chlor mit..... gr. iii
 Sacch lactis..... gr. xx
 M. Ft. chart no. vi.
 Sig.—One as directed. (Mass.)

8

- R. Hydrarg. protoiodid..... ʒ ss
 Potass iodidi..... ʒ ii
 Tinct. cardam comp..... ʒ iii
 M. Sig.—One teaspoonful 4 times a day. (N. Y.)

10

- R. Strych. sulph..... gr. iii
 Liq. arsen. et hyd. iodid.... ʒ i
 M. Ft. sol. Sig.—3 drops in water.
 (Wis.)

12

- R. Cocainæ hydrochlor..... gr. x
 Sodii boratis..... ʒ i
 Zinci sulphatis..... gr. i
 Acidi borici..... ʒ i
 Aquæ rose..... ad. ʒ i
 M. Ft. collyr.
 Sig.—Collyrium. (New Mex.)

14

- R. Acidi nitrohydrochloric.... ʒ v
 Ess. pepsin..... ʒ ii
 Aquæ..... ad. ʒ iii
 (Wash.)

16

- R. Spir. ammon aromat..... ʒ ii
 Liquoris calcis..... ʒ xiv
 Sig.—Tablespoonful for nausea.
 (N. C.)

18

- R. Sodii salicylat..... ʒ i
 Glycerini..... ʒ iss
 Ol. gaulther..... ʒ iss
 Tinct. ferri chlor..... ʒ iss
 Acid citric..... gr. v
 Liq. ammoniæ..... ad. ʒ ii
 M. Sig.—One dessertspoonful two or three times a day. (Mass.)

20

- R. Quininæ sulph..... gr. xlviii
 Fldext. glycyrrhiz..... ʒ iv
 Acid sulphuric dil..... ʒ xxx
 Syrupi..... ad. ʒ ii
 M. Sig.—ʒ i qq. 4 hours. (N. H.)

22

- R. Tinct. aconiti..... ʒ ii
 Spir. æth. nit..... ʒ ii
 Liq. ammoniæ..... ʒ i
 Syr. simp..... ad. ʒ iii
 M. Sig.—One teaspoonful every 4 hours for baby Louise. (Vt.)

- 23
- R. Potass iodidi..... 3 iii
 Fluidext. ipecac..... 7 xx
 Ammon carb..... 3 ii
 Elixir simp..... ad. 3 iv
 M. Sig.—Teaspoonful. (Ga.)
- 24
- R. Tinct. ferri chlor..... 3 ii
 Sodii benzoat..... 3 iss
 Elix. arom..... ad. 3 vi
 M. (Wis.)
- 25
- R. Salol..... 3 iii
 Strych. sulph..... gr. ii
 Pulv. ext. bellad..... gr. xx
 M. et in chart xl divide.
 Sig.—One after meals. (Neb.)
- 26
- R. Codeinæ sulph..... 3 iss
 Terpin hydrat..... 3 iii
 Pulv. ipecac..... 3 i
 M. Ft. caps xl no.
 Sig.—One every 3 hours.
- 27
- R. Atropinæ sulph..... gr. i
 Cocainæ mur..... gr. ii
 Sodii boratis..... gr. vi
 Aq. dest..... ad. 3 i
 M. Ft. collyr.
 Sig.—One or two drops t. i. d. in eye.
 (Tex.)
- 28
- R. Spir. æth. nitrosi..... 3 iii
 Tinct. ferri chlor..... 3 iv
 Mucil acaciæ..... 3 iss
 Glycerini..... 3 ii
 Syrupi..... ad. 3 vi
 M. Sig.—One dessertspoonful q. i. d.
 as directed. (Tex.)
- 29
- R. Morph. sulph..... gr. x
 Bismuth subgal..... 3 i
 M. Ft. pulv. xv no.
 Sig.—One every 6 hours. (Min.)
- 30
- R. Salol..... 3 iii
 Strych. sulph..... gr. ss
 Po. ext. bellad..... gr. x
 M. et in pulv. xv divide.
 Sig.—One after meals. (Min.)
- 31
- R. Santonini..... 3 ii
 Hydrarg. chlor. mit..... gr. xxx
 Sacchari pulv..... 3 ii
 M. et in pulv. xxx no. div.
 Sig.—One at night.
- 32
- R. Hydrarg. iodid rub..... gr. iii
 Potass iodidi..... 3 ii
 Fldest. cinchonæ..... 3 iv
 Syrupi..... 3 vi
 M. Sig.—3 i every 4 hours. (Ill.)
- 33
- R. Potass iodidi..... gr. lx
 Tinct. ferri perchlorid..... 3 iii
 Aquæ..... ad. 3 iii
 M. Sig.—Teaspoonful every 3 hours.
 (Ill.)
- 34
- R. Liq. potass arsenit..... 3 ii
 Syrupi..... 3 i
 Aquæ q. s..... ad. 3 vi
 M. Sig.—A teaspoonful 3 times a
 day. (Ark.)
- 35
- R. Codeinæ sulph..... 5 iss
 Terpin hydrat..... 3 iii
 Pulv. ipecac..... 3 i
 M. et divide in capsul no. xv.
 Sig.—One every 3 hours. (Wash.)
- 36
- R. Ext. belladonnæ pulv..... 5 ss
 Sodii salicylat..... 3 ii
 Misce et in capsul xxiv no. div.
 Sig.—One every 4 hours. (Wash.)
- 37
- R. Ext. nucis vomic pulv..... 3 i
 Sodæ bicarb..... 3 iii
 M. Divide in capsulas v no.
 Sig.—One before meals.
- 38
- R. Morphinæ sulphat..... gr. xii
 Bismuth subnit..... gr. xxx
 Sacchari..... 3 i
 Misce Ft. pulv. xii no.
 Sig.—One every 2 hours. (Ill.)
- 39
- R. Strychninæ sulph..... 2.00
 Potass bromid..... 10.00
 Aquæ q. s..... ad. 90.00
 M. Sig.—Teaspoonful 3 times a day.
 (Ind.)
- 40
- R. Strych. sulph..... gr. xvi
 Tinct. digitalis..... 3 vi
 Spir. ammon. aromat..... 3 iv
 Elix. simpl..... ad. 3 iv
 M. Sig.—3 i t. i. d. before meals.
 (Ind.)

41

- R. Strontii bromidi..... gr. lxxx
 Sodii salicylatis..... gr. clx
 Aquæ q. s.....ad. 3 ii
 M. et ft. sol.
 Sig.—Cochleare parvum ter in die.
 (Ill.)

43

- R. Argenti nitratis..... gr. v
 Liq. formaldehydi..... 3 ii
 Aquæ. destillat.....ad. 3 ii
 M. Sig.—For external use.

45

- R. Strychninæ sulph..... gr. ss
 Kali iodidi..... 3 iss
 Syr. sarsap. co ad. 3 iv
 M. Sig.—One teaspoonful every 3 or
 4 hours as directed. (S. D.)

46

- R. Strychninæ sulph..... gr. i
 Potassii bromid..... 3 i
 Aquæ q. s.....ad. 3 iv
 M. Ft. sol. Sig.—3 i 3 times a day.
 (Ia.)

48

- R. Spir. æth. nit..... 30.0
 Spir. menth pip..... 5.0
 Tr. aconiti rad..... 0.2
 Sat. sol. magnes. sulph ad. 120.0
 M. Sig.—One teaspoonful 3 times a
 day. (Neb.)

50

- R. Morphinæ sulphatis..... gr. ii
 Potass bicarb..... 3 xii
 Aquæ q. s.....ad. 3 ii
 M. Ft. sol. (Id.)

51

- R. Sodii boratis..... 3 ss
 Sodii bicarb..... gr. xx
 Glycerini..... 3 ss
 Aquæ..... 3 iii
 M. Sig.—As directed. (Tex.)

53

- R. Potass iodidi..... 3 iii
 Hydrarg. bichlor..... gr. ii
 Tinct belladonnæ
 Tinct. nucis vom.....aa 3 i
 Aquæ q. s.....ad. 3 iv
 M. Sig.—Teaspoonful in aq. t. i. d.
 a. c. (Ill.)

55

- R. Tinct. ferri chlor..... 3 ii
 Tinct. cinchon. co..... 3 ii
 Tinct gentianæ co.....ad. 3 iv
 M. (Tex.)

42

- R. Morphinæ sulphat..... 0.12
 Sodii boratis..... 0.30
 Aquæ destillat..... 30.00
 M. Ft. solut.
 Sig.—One drop in eye at night.
 (Ind.)

44

- R. Tinct. ferri acetat..... 3 ss
 Tinct. valerianæ..... 3 ii
 Spir. ammon arom..... 3 ss
 Syrupi..... 3 i
 Aquæ.....ad. 3 iv
 M. Sig.—One teaspoonful every 4
 hours. (Okl.)

47

- R. Morphinæ sulph..... gr. ii
 Potass bicarb..... 3 iss
 Aquæ q. s.....ad. 3 ii
 M. Sig.—Teaspoonful when needed.
 (Ia.)

49

- R. Strychninæ sulph..... gr. i
 Potass bromid..... 3 i
 Aquæ q. s.....ad. 3 iv
 M. Ft. sol. (Id.)

52

- R. Liq. potass arsenit..... 3 ii
 Liq. ferri dialysat.....ad. 3 iv
 M. Dose. One teaspoonful. (N. C.)

54

- R. Potass chlorat..... 3 ii
 Acid tannic..... 3 ss
 Glycerini..... 3 i
 Aquæ.....ad. 3 iv
 M. Sig.—Use as directed. (Tex.)

56

- R. Acidi carbolici,
 Sodii boratis.....aa 3 i
 Cocainæ hydrochlor..... gr. xii
 Glycerini..... 3 iv
 Aquæ menth pip.....ad. 3 vi
 M. Ft. sol. Sig.—External use.
 (Tex.)

57

- R. Syr. acidi hydriod. ʒ iv
 Tinct. ferri chlor. ʒ ii
 Glycerini. ʒ iii
 Aquæ. ad. ʒ ii
 M. (N. Y.)

59

- R. Acid sulphuric arom. ʒ i
 Bismuthi subnit. ʒ ii
 Tinct. opii deod. gtt. xxiv
 M. Sig.—Teaspoonful 3 times a day.
 (N. C.)

61

- R. Cocainæ mur. gr. x
 Argenti nitratis. gr. ii
 Aquæ destillat. ʒ iii
 M. Ft. collyr. Sig.—Apply to the
 eyes as required. (N. Y.)

63

- R. Quinina sulph. ʒ iss
 Sodii bicarbonatis. ʒ iv
 Glycerini. ʒ i
 Tinct. ferri chlor. ʒ iv
 Elix. aromat. ʒ ii
 Aquæ q. s. ʒ vi
 M. Sig.—Take as directed. (Wis.)

65

- R. Sodii bicarbonat. ʒ iv
 Bismuthi subnit. ʒ iv
 Tinct. nucis vom. ʒ iv
 Elix. simplic. ad. ʒ ii
 M. Sig.—ʒ i before meals. (Wis.)

67

- R. Tinct. strophanthi. ʒ i
 Sodii iodidi
 Sodii bromidi. aa ʒ iv
 Elix. lact. pepsin. ad. ʒ iii
 M. Sig.—ʒ i in aq. q. hora ter.
 (N. C.)

69

- R. Kali iodidi. ʒ ii
 Strychnina sulph. gr. 3/4
 Liq. kali arsenit. ʒ iss
 Aq. lauroceras. ad. ʒ iii
 M. (Pa.)

71

- Natrii salicylatis. 3.0
 Liq. morphina sulph. 30.0
 Syrupi rhei. 15.0
 R. Aquæ q. s. ad. 120.0
 M. Sig.—Capiat cochleare parvum
 omni tertia hora. (N. Y.)

58

- R. Strychnina sulph. gr. i
 Tinct. belladonna. ʒ ii
 Liq. iodi comp. ʒ ii
 Aquæ. ad. ʒ iv
 M. Sig.—ʒ i in aq. t. i. d. (Fla.)

60

- R. Antipyrin. ʒ iss
 Spt. æth. nitros. ʒ i
 Aquæ q. s. ad. ʒ ii
 M. Ft. sol. Sig.—ʒ i p. r. n. (Fla.)

62

- R. Bismuthi subcarb. ʒ ii
 Pepsini. ʒ i
 Acidi hydrochlor dil. ʒ ii
 Syr. aurantii. ʒ iv
 Acid hydrocyan. dil. ʒ iss
 Aq. menth pip. ad. ʒ iv
 M. Sig.—Tablespoonful at bedtime.
 (Br. Col.)

64

- R. Cocainæ mur. gr. iv
 Sodii boratis. gr. iii
 Glycerini. ʒ ii
 Aquæ destillat. ad. ʒ i
 M. Sig.—Drop in eye three times a
 day. (Wis.)

66

- R. Sodii salicylatis. 4.0
 Fldest cascaræ sag. 3.0
 Mist. rhei et sodæ. ad. 90.0
 M. Sig.—8 t. i. d. p. c. (N. Y.)

68

- R. Potass iodidi. ʒ iii
 Hydrarg bichlorid. gr. ii
 Tinct. belladonna
 Tinct. nucis vom. aa ʒ i
 Aquæ. ad. ʒ iv
 M. Sig.—Teaspoonful in aq. t. i. d.
 p. c. (Fla.)

70

- R. Syr. ferri iodidi. ʒ iv
 Liq. potass arsenit. ʒ iii
 Sodii salicylat. ʒ iv
 Syr. pruni virg. ʒ iv
 Ess pepsin. ad. ʒ iii
 M. Sig.—ʒ i in aq. t. i. d. (N. C.)

72

- R. Sodii salicylat
 Quinina sulph. aa gr. xx
 Syr. zingiberis. ʒ ii
 M. Sig.—Teaspoonful every 3 hours.
 (N. C.)

73

R. Acid chromici..... gr. xx
 Glycerini..... ʒ i
 M. Ft. sol. (Tex.)

75

R. Tinet. nucis vomic..... ʒ i
 Acid nitromuriat..... ʒ iv
 M. Sig.—10 drops as directed. (Tex.)

77

R. Potass. permanganat..... gr. xxx
 Glycerini..... ʒ i
 Ft. sol. Sig.—As directed. (Mich.)

79

R. Sat. solut. potass iodid..... ʒ i
 Sig.—Ten drops as directed. How
 much iodide per dose? (Mich.)

74

R. Nitroglycerin..... gr. v
 Potass iodidi..... ʒ iv
 Sodii bromid..... ʒ v
 Flidext sarsap..... ad. ʒ iii
 M. Sig.—ʒ i in aq. q. 4 hrs. (N. C.)

76

R. Phenolis..... ʒ i
 Collodii..... ʒ i
 S. A. Sig.—Apply as directed.
 (Mich.)

78

R. Potass. citrat..... ʒ ii
 Spir. aeth. nit..... ʒ i
 Syrupi..... ʒ i
 Aquæ..... ʒ i
 M. Ft. sol. (Mich.)

80

R. Antipyrinæ..... ʒ i
 Sodii salicylatis..... ʒ i
 M. Ft. chart No. xii. (Mich.)

KEY TO STATE BOARD PRESCRIPTIONS

It is impracticable to thoroughly discuss all phases of the prescriptions given, so only the most important points are considered.

State Board prescriptions usually aim to disclose the candidate's knowledge and observation regarding (A) over-doses, (B) recognition of official preparations when written in modified formulas, and (C) general knowledge of incompatibilities and skill in compounding. This key points out in each case the essential feature, and gives some suggestions under C which are more fully explained in the text of the book.

The first figure refers to the number of the prescription; the others to the ingredients in the order of writing.

MIXTURES (CHAPTER IV)

1. 1 insoluble, 2 with tannin in 5.
2. Quantities of 2, and 3 reversed.
3. Dissolve separately and mix (saves time).
4. 1 with tannin in 2 (color).
5. 1 and acid in 3 with 2.
6. 1 and 3 may ppt.
7. 1 and 2 (overcome by 3 and 4?).
8. How compounded? (U. S. P. Solution).
9. 1 and alcohol in 3 and 4 (separation).
10. 1 and 2 (color).
11. How much 2 and how used?
12. 1 and 2; alcohol and glycerin may prevent ppt.
13. Pharmaceutical treatment of 1 and 4?
14. 3—synonym for?
15. Pharmaceutical treatment of 1, 2 and 4?
16. How compound?
17. 5 may discolor with 1. How prevented?
18. Black Wash with tragacanth.
19. 1 discolors with 3; 2 and 3 incompatible, overcome by 4.
20. 1 and 3 effervesce; also acid in 4.
21. Method of compounding?
22. Method of compounding?
23. 3 and 4 incompatible.
24. 1 and 2 may react. How compound?
25. Calculation.
26. 2 reacts slowly with 1 in water, and with acid in 3.
27. How dissolve 1, 2 and 3?
28. Calculation.
29. How use 2?
30. 4 colored by 1 and 3; 1 and 2 may prevent ppt. of 4 by 6.
31. 2 may ppt. 1. (Alcohol in 3 may prevent?)
32. 1 and 2 make alkaloidal pptnt. for 3; alcohol may prevent.
33. How dissolve 2 and 3?
34. 2 and 3 insoluble; how treat?
35. Decomposition products in 3 may react with 1 and 2.
36. Compare with 32.
37. 1 ppts. 3 and 4; also reacts with 2. How compound?
38. How compound?
39. 1 is soluble in 4, but pptd. by alcohol in 2 and 3 (2 might be syrup?).

40. Basham's Mixture, U. S. P.
41. Acid in 3 reacts with 1. How compound?
42. 2 ppts. 1. Purpose of 3?
43. Oil in 1 thrown out by 2 and 3.
44. 3 may discolor 2 in solution. How compound?
45. See page 57.
46. Iodine likely to be liberated slowly by infusion.
47. 2 discolors 1.
48. 1 and 2 liquefy. Better dissolve successively.
49. Liniment of ammonia—old form.
50. Calcium citrate may precipitate.
51. How treat 2?
52. 1 dissolves slowly and reacts slowly with acids in (2) 3 and 4.
53. Compare 44.
54. Solution of 2 and 3 dissolves 1.
55. Dissolve 1 in 60 m. alcohol and mix with 3iii collodion.
56. Calculation.
57. Solution of potassium citrate U. S. P.
58. Mix 2 and 3, then add 1 and lastly 4. May cloud.
59. Compare 45.
60. Dissolve 2 in 3 before adding 1.
61. Some prefer a suspending agent—some not.
62. How dissolve 1 and 2?
63. 1 and 2 mutually incompatible. Large dose of 2. Questionable.
64. Calculations.
65. Doses?
66. 2 reacts with 1 and ppts. 3. Use spirit of ammonia if compounded.
67. 1 and 2 slight effervescence with 3. Probably no ppt.
68. 1 ppts. alkaloids in 2 and 3.
69. How dissolve 1 (use warm water 3i).
70. 1 is not soluble. Triturate with cold solution of 2 and 3.
71. Doses?
72. 1 will destroy pepsin.
73. Oil in 1 thrown out by 2 and 3. Cloudy mixture.
74. Explosive. Do not compound.
75. 2 ppts. 1, but 3 may hold in solution. How mix?
76. U. S. P. Solution of Arsenous Acid.
77. Acids in 2 and 4 incompatible with alkali in 3.
78. 2 separated from solution by 1 and 3. Shake mixture.
79. Triturate 1 with 4, add 5 then the rest. Shake.
80. 1 and 2 may react. How compound to prevent?
81. Calculation. 1 and 2 form double salt.
82. Calculation.
83. 1 incompatible with all others.
84. Griffith's Mixture (compound iron carbonate mixture).
85. (See 58.)
86. 1 pptd. by 3. (Use 5 m. glycerin, or boric acid.)
87. 1 not entirely soluble. Powder and incorporate (see No. 11, page 461. Also how incorporate 2.)
88. 2 ppts. alkaloids and tannoids in 1. Shake.
89. Rub together 1 and 4, and incorporate the rest in order.
90. 1 not entirely soluble in 3. Shake.
91. Calculation. (Compare 82.)
92. 1 and 2 pptd. by 3. Use 5 minims of glycerin.
93. See page 57.
94. Effervesces when mixed. Add glycerin last.
95. Dissolve 1 in all of 3 and add 2 slowly.
96. Suspend 2 by means of gum. (See No. 9, page 152.)
97. Calculation.
98. Dissolve separately and mix. (White Lotion.)
99. Modified Black Wash.
100. 2 reacts with 5, and slowly with 1. Color changes.
101. 1 and 2 pptd. by 3. Shake mixture.
102. 2 darkened by 1. Citrochloride better.
103. 4 liberates iodine from 1. Citrochloride better.

104. Dissolve 1 in 5, add 4, then 2 and slowly 3.
105. 2 and 3 decompose 1 slowly. Effervesces.
106. 3 liberates iodine from 1. Use citrochloride.
107. Quinine acetate (very bulky) formed. (Glycerin may help.)
108. 1 darkened by 2. Citrochloride not darkened.
109. Compare Basham's Mixture.
110. Basham's Mixture.
111. Over-dose of 1.
112. Over-dose of 1. 2 thrown out by 4.
113. Calculation.
114. Double dose of 1 and 2 is too much.
115. Over-dose of 1.
116. Method of mixing.
117. Black Wash.
118. Dissolve separately and mix. Shake mixture.
119. See No. 118.
120. Black Wash.
121. 2 incompatible with 1, but partly overcome by 3.
122. Effervesces. How much of 2?
123. Acids in 2 and 3 cause slow effervescence with 1.
124. 5 is immiscible with others. Use 9 m. creosote and 3 ounces of 4.
125. Needs an emulsifying agent.
126. 3 not miscible entirely. Use 1.2 Gm. benzoin.
127. 3 is insoluble. Use equivalent of cocaine alkaloid.
128. Calculations.
129. Calculations.
130. Emulsifying agent needed.
131. Add 2 last and very slowly. Honey or mucilage would improve it.
132. 3 is immiscible. Spirit of ammonia better to use.
133. 3 is immiscible. Spirit of ammonia needed.
134. 2 slowly decomposes and iodine combines with 1.
135. Effervesces. Excess of 2 decomposes 4.

ADJUSTED SOLUTIONS (CHAPTER V)

1. 2 ppts. 1, but 4 may prevent it.
2. 3 buffers acid in 1 and throws out caffeine.
3. Use cocaine alkaloid.

EMULSIONS (CHAPTER VI)

1. Use 12.5 Gm. powdered acacia.
2. Use 1.5 Gm. powdered tragacanth. (See 27, p. 144.)
3. Use 20 grs. powd. acacia, or 8 grs. powd. tragacanth.
4. Mix the castor oil with the oleoresin and emulsify.
5. Emulsify 1 by gradual trituration with 3 and add 2.
6. Mix 1, 2 and 3 and gradually add 4.
7. Mix, 1, 2 and 3 and gradually add 4. (60 grs. po. acacia would improve it.)
8. Use 2 drachms powdered acacia.
9. Mix 2 and 3, add 0.4 Gm. powd. tragacanth, then the water.
10. Mix petrolatum, oil and gums and gradually triturate with water.
11. Add tincture last, very slowly, and with agitation.
12. Treat as turpentine emulsion.
13. See Nos. 2 and 6. (Also U. S. P. IX.)
14. Mix oils and acacia, add 30 cc. water, emulsify and dilute.
15. Use 2 drachms powd. acacia. (See N. F. V.)
16. Use 12.5 Gm. (or 6.25 Gm.) powd. acacia.
17. Acacia and lime water interfere. Use distilled water in place of lime water.
18. Can be emulsified with either acacia or tragacanth.
19. Make according to rule.
20. Emulsify terbene with 2 Gm. acacia, and mix extract with syrup before adding to emulsion.
21. Dissolve camphor in oil and emulsify with po. acacia. Add elixir containing benzoate last.

22. Potass. acetate and syrup together interfere with emulsification. Make emulsion with oil, po. acacia and water, and add acetate and sugar in diluting water.
23. Mix oil and acacia and add 26 water. Emulsify and dilute.
24. Use 6 Gm. acacia, emulsify and dilute.

PILLS (CHAPTER VIII)

State Board prescriptions for pills are mostly for observation of the candidate's method of mixing and deftness in handling the mass and finishing the pills. The choice of excipients is rarely of primary importance, except when chemical action may be involved.

1. Heavy doses of 1 and 3. Mix pilular extracts first, add powders, then mass.
2. Mix 2 and 3, incorporate 1 and mass.
3. Treat in same manner as camphor or chloral, but avoid soap.
4. Make white pills.
5. Mix with about 12 grains of starch or lactose and make white pills.
6. Practice in mixing and massing.
7. Adhesive excipient best.
8. Quantities of 2 and 4 are probably reversed.
9. Mix 1, 2 and 3 successively with 4 to insure thorough admixture.
10. Mix 1 and 3 and add 2, or use equivalent of solution for syrup.
11. The mass of ferrous carbonate is best made after mixing in the arsenic.
12. Rather a difficult combination to mix well.
13. May involve calculations on 4.
14. Alcoholic excipient will make smaller pills.
15. Care in mixing and also in adding excipient.
16. See No. 12.
17. Care in mixing.
18. Aqueous excipient will make effervescent pills, by slow reaction.
19. Method of mixing and calculation involved in 5. Latin
20. Latin translation.
21. Slow reaction if aqueous excipient is used.
22. Alcoholic excipient will make small pill.
23. Bland's Pills with arsenic. Latin important.
24. Weighing and mixing (of 2 particularly).
25. Excipient important.
26. Mixing important.
27. Method of mixing. Heavy dose of 1.
28. Over-dose of 1.
29. Methods of weighing, mixing and calculations.
30. Calculations and mixing.
31. Bland's pills with arsenic. Calculations and method.
32. Latin and technique.
33. See text on permanganate in pills.
34. 4 is of doubtful value. Make as small pills as possible.
35. Dose of 1 heavy. Over-dose of 3.
36. Quantities probably reversed.
37. Latin and technique.
38. 1 and 2 liquefy. Absorbent needed.
39. Method of mixing and massing.
40. Bland's pills (see U. S. P.).

TABLETS AND TROCHES (CHAPTER X)

1. Technique.
2. Care in mixing and technique.

POWDERS, CAPSULES, ETC. (CHAPTER XI)

State Board prescriptions for these usually are designed to show the candidate's knowledge of materials in the methods employed for powdering and mixing. Eutectic mixtures are frequent and cannot always be foretold--especially when three or more ingredients are concerned.

1. Heavy trituration may cause a reaction.
2. Alcohol or ether needed to powder 2.

3. 2 is darkened by 1 if moist or by heavy trituration.
4. 1 and 3 become damp when rubbed together.
5. Mix lightly. Explosive by friction or pressure.
6. Salol is troublesome to mix.
7. Mix 2, 3 and 4 and add 1 lightly.
8. 1 must be mixed cautiously.
9. 1 and 2 liquefy. Not practical for powders.
10. Very questionable dose of santalin.
11. Liquid. Use soft capsules.
12. Weighing and mixing. Latin.
13. Over-dose of 1. Method of mixing.
14. In soft capsules a little fixed oil is needed to prevent leaking.
15. Manipulation. Avoid taste on outside of capsules.
16. Salol difficult to powder and mix.
17. Mix cautiously. Powdering of salol.
18. 1 and 2 will react slowly, and soften. Mix cautiously.
19. Over-dose of belladonna.
20. If mass is made, care in mixing arsenic.
21. Over-dose of nux vomica. (Error in number of capsules?)
22. Dissolve the salol in the castor oil.
23. Add fixed oil to prevent leaking in soft capsules. (See No. 14.)
24. Triturate lightly to prevent reduction of 1.
25. Weight equivalents and size of capsules.
26. Becomes pasty when mixed. Dry or add starch.
27. How much per powder? Latin translation.
28. Powdering salol. (See No. 6.)
29. Method of mixing.
30. Use dried alum in proportion, to keep pulverulent.
31. Excessive dose of morphine.
32. 1 and 2 liquefy. Use dry starch.
33. 3 destroys activity of 1. Mix lightly. Latin.
34. Mix cautiously. Possibility of becoming pasty.
35. Over-dose of 1. (Quantities of 1 and 2 probably reversed.)
36. Slowly becomes pasty and 2 is changed to quinine. (May dispense.)
37. Method of mixing and size of capsules.
38. 1 and 2 soften. Over-dose of 5.
39. Method of mixing. Questionable dose of 2.
40. Interpretation of 2 and method of mixing.
41. Mix lightly.
42. 2 is very deliquescent. Absorb in starch but avoid magnesia.
43. Method of mixing. Latin translation.
44. Method of mixing.

SUPPOSITORIES (CHAPTER XII)

1. Iodoform and camphor soften cacao butter. Spermaceti or wax is needed.
2. Phenol softens cacao butter. Spermaceti needed. Caution with 1.
3. Thymol iodide is soluble in cacao butter. Caution with 1.
4. Manipulation.
5. Mix tannin with cacao butter, and extract with cacao butter separately.
6. If made cold treat as 5, if by hot process usual precautions.
7. Sulphur partially dissolves in hot cacao butter.
8. Spermaceti or wax needed.
9. Mix cautiously by hot process; and pour when thick.
10. Spermaceti or wax needed.
11. Caution in incorporating belladonna by hot process.

OINTMENTS (CHAPTER XIII)

1. 1 and 2 should be incorporated separately at first.
2. Rub to smooth ointment (see 50, above).
3. Calculation and incorporation of yellow oxide (rub with oil).
4. Old official potassium iodide ointment.
5. Method of mixing. (Mix 3 and 4 first.)
6. Heat 1 with 2 until combined, add 3 and 4 successively.
7. See 5.

8. Triturate 1 with small portion of 2 until extinguished.
9. Triturate 1 with a little of melted 3 first.
10. Smooth ointment.
11. Mix 1 with 2, and 3 with 4, then mix together.
12. Warm 1 with 2 until dissolved, then add 3.
13. Strength and method of mixing. (See N. F. V.)
14. Dissolve 2 in 3, add 1 and incorporate 4.
15. Soften 2 with 3, and incorporate with 4, then add 1 and 5.
16. Powder 2 and 3 very finely before mixing. (Use no water.)
17. Dissolve 1 in 40 min. water before mixing and add thiosulphate.
18. Dissolve 1 in water, incorporate with part of 4, then add the rest. Latin.
19. Triturate 3 with 2 and incorporate with the rest. Latin.
20. Spreading.
21. Dissolve 2 in 2 m. water and mix with 3. Mix 1 with 4 (s. a.) and mix the two ointments.
22. Needs 10 grs. potassium iodide.
23. Make smooth ointment.
24. Calculations.
25. Smooth ointment.
26. Powder 3 finely, add 4, 2 and 1, then 5, successively.
27. Calculation and choice of base.
28. Mix 3 with 3ii alcohol, add 4 and 5, then 1 and 2.
29. See 21.
30. Mix 2 and 4 with 3ii alcohol, add 5; then 1, 2 and 6.
31. Calculation and need of thiosulphate.
32. Dissolve 3 and 4 in 1 (warm) and add 2.
33. Triturate 1 with 4, then add 3 and lastly 2.

MISCELLANEOUS EXTERNAL PREPARATIONS (CHAPTER XIV)

1. See N. F. Calculations.
2. Mercuric oleate.
3. Dissolve in succession to obtain clear solution.

INCOMPATIBILITIES (CHAPTER XVIII)

1. 1 and 3 incompatible. (Use 5 min. glycerin with 3.)
2. Dissolve 2 and 3 separately and mix. (Lead sulphate pptd.)
3. 1 slowly reacts with acids in 2 and 3.
4. 4 gives colors with 1, 3 and 6.
5. 1 is incompatible with all the rest (explosive).
6. 2 and 3 are incompatible. Shake mixture.
7. 1 is oxidized by 3, and 3 gives red color with 2.
8. 1 is changed to mercuric iodide by 2. Toxic dose. Water needed.
9. Forms bismuth oxyiodide (yellow, red or gray).
10. 1 is precipitated by 2.
11. Chloral alcoholate may form. 1 not entirely soluble. Add 3 last.
12. 2 precipitates both 1 and 3. Use glycerin—20 minims.
13. 1 slowly reacts with acids in 3 and 4. Fldext. may be intended for 2.
14. 1 destroys activity of 2, and is itself reduced.
15. Ferric hypophosphite is pptd. (soluble in hypophosphorous acid).
16. Calcium carbonate pptd. by 1.
17. 1 pptd. by 2. Shake mixture.
18. 4 gives color with 1 and 3. 6 probably intended for liq. ammon. acet. (See No. 4.)
19. 1 and 2 pptd. by 3. Use boric acid, or glycerin—6 min.
20. See No. 6.
21. Dangerous dose of 1.
22. Over-dose of 1. 3 decomposes 2. Liq. ammon. acet. probably intended for 3.
23. 1 and 3 both ppt. alkaloids in 2, but alcohol in 3 prevents.
24. 1 pptd. by 2. Shake mixture.
25. Very questionable doses of both 2 and 3. How powder 1?
26. Over-dose of 1.
27. 3 ppts. both 1 and 2. Use 6 m. glycerin, or boric acid.
28. 3 is pptd. by both 1 and 2. See page 57.
29. Questionable dose of 1.

30. Over-dose of 2 (compare 25).
31. Over-dose of 1 (compare 21).
32. 1 and 2 form precipitant of alkaloids in 3.
33. 2 liberates iodine from 1. Do not dispense.
34. Over-dose of 1. Probably 5ii intended.
35. Over-dose of 1.
36. Over-dose of 1.
37. Over-dose of 1.
38. Over-dose of 1.
39. Over-dose of 1. 2 will ppt. 1 from solution.
40. Over-dose of 1. 3 ppts. 1 and destroys activity of 2.
41. 2 ppts. strontium salicylate.
42. 2 ppts. 1. Use 5 min. glycerin, or boric acid.
43. 1 is reduced by 2. Do not dispense.
44. 3 ppts. 1.
45. See 17.
46. 1 is pptd. by 2 (compare 39 and 49).
47. 2 ppts. 1. Not safe for a shake-mixture. (Potass. hydroxide would redissolve.)
48. Alcohol in 1, 2 and 3 ppts. magnesium sulphate.
49. Compare 39 and 46.
50. Compare 47.
51. 1 reacts with 3 and causes effervescence with 2.
52. 1 and 2 incompatible. 2 absorbs and antidotes 1.
53. 1 and 2 form precipitant for alkaloids in 3 and 4. Excessive dose of 3.
54. Method of mixing. Avoid triturating 1 with 2 and 3. 1 not entirely soluble, must be powdered alone.
55. Inky mixture. Tinct. citrochloride of iron makes a better mixture.
56. Triturate 2 with 4 to overcome incompatibility with 3.
57. 2 liberates iodine from 1. Not suitable for dispensing.
58. 3 ppts. alkaloids of 1 and 2. Doubtful if it should be dispensed.
59. Prescription unfinished. Impracticable mixture as written.
60. Mixture turns green. May be dispensed.
61. 1 and 2 incompatible. (See page 446, R 42.)
62. 3 and acid in 4 cause effervescence with 1. Over-dose of 5.
63. 2 ppts. 1 and 4. Use tinct. ferric citrochloride. Shake mixture.
64. 3 overcomes incompatibility of 2 with 3.
65. 1 not entirely soluble, and reacts slowly with 2. (Dose of 3?)
66. Slight effervescence of 3 with natural acids in 2.
67. Large over-dose of 1. 2 and 3 not entirely soluble. Iodine may be slowly liberated.
68. 1 and 2 form precipitant for alkaloids in 3 and 4. Excessive dose of 3. (Compare 53.)
69. 1 and 3 both ppt. 2. Unsafe shake mixture.
70. 2 may ppt. ferrous carbonate. Mix 2 with 4 and 5 and neutralize mixture, if necessary, before adding 3 and 1. Excess of acid ppts. 3.
71. Alkali in 3 ppts. morphine and slowly darkens 1.
72. Quantity of 3 probably intended for 5ii. Quinine salts insoluble.
73. Explosively inflammable. Not safe.
74. Over-dose of 1, and also insoluble.
75. Mutually incompatible. Each largely decomposed.
76. 1 coagulates 2. Mix very slowly and cautiously.
77. Explosive mixture. Do not dispense.
78. Nitrous ether driven out.
79. N. F. preparation. Calculation.
80. Eutectic mixture:—liquefies. How dispense?

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